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# ELEMENTARY ILLUMINATION FOR THE OPHTHALMOLOGIST

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Poor illumination produces ocular symptoms. The ophthalmologist is frequently consulted with regard to these symptoms, and he should be able to recognize and treat them effectively. He should, in addition, be prepared to do his part in preventing, as well as in ameliorating, conditions which might cause such symptoms.

The scope of such activities may vary from simple, obvious advice to full scale cooperation with the illuminating engineer, the architect and the decorator. With his understanding of individual differences and needs, his freedom from commercial bias and his awareness of the part played by good lighting in the comfort and welfare of the eyes, the ophthalmologist occupies an important position in this phase of public health service. The purpose of this brief report is to outline the basic facts and principles of good lighting so that the ophthalmologist may be well guided in his individual or cooperative efforts to alleviate or avoid distress arising from defective illumination.

## LIGHTING TERMS AND UNITS

The ophthalmologist is not concerned with the rigid mathematical and operational expressions used by radiation engineers. To him lighting is the science of creating and distributing light, which he describes as radiant energy evaluated according to its capacity to produce visual sensation. Since all practical sources of light include neighboring bands of radiations (infra-red or ultraviolet), these portions of the spectrum are included in his considerations as coincidental factors and are evaluated physiologically. Light (a temporal concept) and illumination (an areal concept) are not differentiated. One may overlook this lack of rigor, without condoning the meaningless phrase "foot candle power," so often encountered in ophthalmologic writings.

It will greatly facilitate the problem for the ophthalmologist if he will adopt three simple concepts:

1. *Source.*—The source of light is evaluated in terms of power of which the candle (c) is the unit.

*Illumination.*—The illumination at the working plane is evaluated chiefly with reference to the distance of the working plane from the source.

3. *Brightness.*—This term, again a power term, may refer to the source itself (intrinsic brilliance, expressed as candles per square centimeter or per square inch or per square foot) or to light reflected toward the eye from an object.

Simple units to express measurements of these three factors may now be derived.

*Source.*—The candle is the unit of luminous intensity. As a power term it expresses the intensity of the source. It is an antiquated concept, dating from the earliest attempts at evaluation and control of lighting. The old English sperm candle (six to a pound), which burned at the rate of 120 grains of spermaceti per hour, was taken as a standard. This standard has now been conserved by international standardizing laboratories in terms of incandescent lamps.

This candle flame emits luminous, or light, flux in all directions. The amount of this light flux encompassed in a unit solid angle (steradian) is the unit called a lumen. If the candle flame is condensed to a point and this point is situated at the center of a sphere with a radius of 1 foot, the amount of light falling on 1 square foot of the sphere is 1 lumen; and since the area of such a sphere is $4\pi$ square feet, there must be $4\pi$, or 12.57 lumens, emitted by 1 candle.

*Illumination.*—Illumination is the intensity of concentration of light falling on a particular surface, and one unit of measurement is the foot candle (ft. c). The foot candle is defined as 1 lumen per square foot. In the example chosen, since every part of the sphere is 1 foot away from a source of 1 candle power, each square foot of the sphere receives 1 lumen, and the illumination is 1 foot candle.

If the surface were not spherical, but were a plane tangent to the sphere, the illumination

From the Knapp Memorial Laboratories, Institute of Ophthalmology.

would be 1 foot candle only at one point on the plane, and it would be less than 1 foot candle on all other points, the intensity depending on the distance from the point source of 1 candle power and the angle of incidence.

It is thus seen that the illumination (which means intensity of light flux, and hence the phrase "intensity of illumination" is redundant) varies with three factors: the power of the source, the distance from the source and the angle of incidence. However, these three factors operate differently. It is worth remembering that the illumination varies directly with the power of the source; that is, if a 2 candle power lamp is substituted for a 1 candle power lamp, the illumination is doubled. This is a direct proportion.

The variation with distance is not direct; illumination is inversely proportional to the square of the distance from the source. This is the inverse square law, applicable to all radiation, and it means that in order to obtain the same illumination at 2 feet as at 1 foot the power of the source must be increased by $2^2$; or, again, a 100 candle power lamp which gives an illumination of 100 foot candles at a distance of 1 foot gives at a distance of 2 feet only $\frac{100}{2^2}$, or 25, foot candles, at a distance of 5 feet $\frac{100}{5^2}$, or 4, foot candles and at a distance of 10 feet $\frac{100}{10^2}$, or 1, foot candle. This is an important consideration and is the chief reason for supplementing general room illumination with local fixtures. It should be noted in passing that the inverse square law applies rigidly only to point sources and practically is valid only for long distances when large sources are used. It is invalid when the distance is less than five times the dimension of the source. Thus, the illumination from large luminaires or from nearby tubular lamps needs to be measured, rather than calculated.

Finally, if the light does not strike the surface perpendicularly but is incident at an angle, the same amount of flux is distributed over a larger area, and the illumination consequently decreases. The amount of the decrease can readily be shown to be equal to the cosine of the angle of incidence. This is known as the cosine law.

*Brightness.*—It is obvious that only the light which enters the eye is useful for seeing and that unless one is looking at self-luminous objects this light must be reflected. The amount of light reflected from an object will vary with the amount of light incident on it and with its physical characteristics (reflectance). A white object with high reflectance will appear brighter under a given illumination than a dark object with low reflectance. The ratio (percentage) of the amount of light reflected from an object to the amount of light incident on the object is a measure of its reflectance and determines its brightness.

The simplest expression of brightness in terms of the units we have derived is the apparent foot candle. If an object is illuminated with 100 foot candles and has a reflectance of 80 per cent, 80 of these 100 foot candles will be reflected back, and the object will have a brightness of 80 apparent foot candles. In England the term equivalent foot candles is used. Or brightness can be expressed in terms of lumens per square unit of area. If 1 lumen is emitted or reflected from each square centimeter, the area has a brightness of 1 lambert (L). This is very high brightness, and for most practical situations a smaller unit is desired. Such a unit is the millilambert (mL), or 0.001 lambert. If the unit area is taken as the square foot, a surface emitting or reflecting 1 lumen per square foot has a brightness of 1 foot lambert (ft. L). Since there are 1,076 sq. cm. in 1 square foot, the foot lambert equals 1,076 millilamberts, that is, the foot lambert, the millilambert and the apparent foot candle, as expressions of brightness, are practically interchangeable.

A point which often puzzles the ophthalmologist is why the brightness of an object does not noticeably decrease as one recedes from it. We have frequently been asked, for example, what the illumination of a test chart is to a patient 20 feet (6 meters) away. It is a fact that brightness as a sensation does not obey the physical law of inverse squares, but is practically independent of the viewing distance. The explanation of this is that the size of the retinal image varies inversely as the square of the distance, just as does the amount of light reflected from the object. The two are thus in compensating relationship, and the unit density of light in the retinal image is independent of distance for a constant size of pupil. In other words, with increase of viewing distance the smaller amount of light entering the eye is concentrated into a proportionately smaller retinal image, and the projected image is therefore of approximately the same brightness whatever the viewing distance. There should be little change of brightness for different distances of viewing if the size of the pupil of the eye is maintained at these distances.

In estimating illumination the beginner may be perturbed by the fact that whereas the units and principles so far discussed use the candle as a basis of power, most lamps at present are rated

in terms of watts. This difficulty can be lessened by considering the rated luminous efficiency of lamps and the luminous efficiency of the candle. Most incandescent sources used at present for illumination are tungsten filament, gas-filled (type C) lamps. They are rated both in watts per spherical candle power and in lumens per watt. The lumens per watt rating is about 11.5 for the 75 watt size, 14 for the 100 watt size and 16.1 for the 500 watt size. Since the most commonly used lamps are the 75 to 100 watt sizes, 12.5 lumens per watt may be taken as a rough average. As has previously been noted, a standard candle emits $4\pi = 12.57$ lumens; hence in this range (75 to 100 watts) 1 watt may be taken as equal to about 1 candle power. Such approximations as we have suggested are frequently used in illumination surveys, in which precise calculations are neither worth while nor desirable. After all measurements or estimations have been made, it is usual to add as much as 50 per cent to estimated requirements because of the progressive deteriorating influence of soiled walls, ceilings and other reflecting surfaces, the gathering of dirt on bulbs and fixtures and the loss of efficiency due to aging of lamps.

The elementary concepts of lighting units and terms may be summarized thus:

1. Sources of light are rated in power terms, the unit of which is the international candle. Light sources are rated in terms of candle power or watts. For 75 to 100 watt type C lamps, 1 watt is roughly equal to 1 candle power.

2. Luminous flux is a photometric quantity, the unit of which is 1 lumen. One lumen is defined as the quantity of light required to illuminate 1 square foot to an average intensity of 1 foot candle.

3. Illumination is a photometric quantity, expressed in terms of lumens and areas.

1 lumen per quare foot = 1 foot candle (ft. c)
1 lumen per square meter = 1 lux (lx)
1 lumen per square centimeter = 1 phot (ph)
1 foot candle = 1.076 milliphots = 10.7 lux

4. Brightness is a photometric quantity, expressed in terms of lumens and areas. Its unit is the lambert, defined as the brightness of a perfectly diffusing surface emitting 1 lumen per square centimeter.

1 lambert = 1,000 millilamberts (mL)

An apparent foot candle, an equivalent foot candle and a foot lambert are terms for brightness describing the brightness of a perfectly diffusing surface emitting 1 lumen per square foot.

1 foot lambert
1 apparent foot candle } = 1.076 millilamberts
1 equivalent foot candle

5. Intrinsic brilliance is a photometric quantity, expressed in terms of candle power and area. Its unit is the candle power per square inch. It is usually applied to source or transmitted light, rather than to reflected light.

## PHOTOMETRY

The measurement of illumination is based fundamentally on the inverse square law of spread of illumination (fig. 1). Two fields are presented to the eye for comparison, the illumination of one of which is known and that of the other is to be measured. By a comparison of the squares of the distances of the two sources, it is a simple matter of arithmetic to compute the value of the unknown illumination. Adjustment is made of the distance of one of the two sources of illumination until the two fields

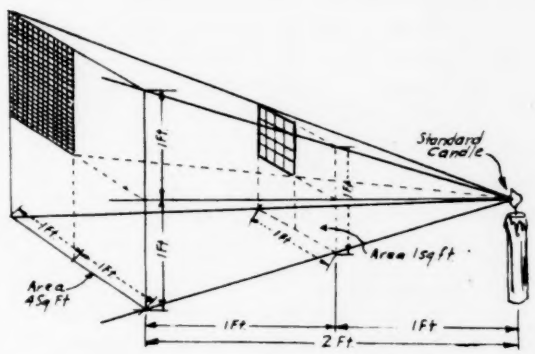


Fig. 1.—Diagram illustrating the inverse square law. The amount of light received on a surface 2 feet distant from a standard candle is $\frac{1}{2^2}$ or one-fourth (¼) the amount received at 1 foot.

are judged to be of equal brightness. Various illuminometers with calibrated scales are on the market for making these measurements readily, the best of which from a practical point of view is the Macbeth illuminometer. Still more convenient, if less accurate, are the various light meters, based on the reaction of the photoelectric cell to intensity of light. These can be used for a rough measure of the illumination at any plane, but since they are not provided with a checking device and their response to intensity of light varies with age and use, they cannot be relied on for more than a rough estimate without being frequently rechecked. Also, they are not applicable to light of a spectral composition differing from that for which they were calibrated. It cannot be denied, however, that they provide a convenient "vest pocket" means of obtaining an approximate estimate of the illumination given by tungsten lamps, for which they are customarily calibrated. Owners of a photoelectric photometer

should be cautioned that such an instrument is an extremely delicate mechanism which should be handled gently. Failure to heed this caution will soon result in an instrument which is badly out of adjustment. With gentle treatment and frequent calibration against known standards, these devices serve a useful purpose.

## ILLUMINANTS

Practically all light comes from one of two sources: incandescent bodies and luminescent bodies. By far the greater portion of light used at present comes from incandescent sources. This includes sunlight, electric filament lights, arc lights and all flame sources. Such light is accompanied by a high percentage of infra-red radiation and, the amount depending on its temperature, some ultraviolet radiation. All hot bodies are inefficient sources of visible radiation.

Luminescence—light from cold bodies—is the only efficient source of visible radiation. Luminescence may be classified as follows:

1. Electroluminescence, light from cathode rays, at present is not important except for special work. This source will probably be of greater importance in the future.

2. Triboluminescence, light produced by friction and crushing, is of no practical importance.

3. Chemoluminescence is light arising from chemical action, such as the bioluminescence of fireflies and sea animals. The oxidation and reduction of the luciferin-luciferase system holds promise of future application to human needs.

4. Photoluminescence, light produced by transformation from short wave radiations into visible radiations, includes fluorescence (light produced during activation) and phosphorescence (light continuing after activation has ceased).

The most widely used form of luminescence is exemplified in the present fluorescent tube lamps, introduced in 1938. These consist essentially of a glass tube with an electrode sealed in each end. An arc is produced by current flowing between these electrodes through mercury vapor contained within the tube when the lamp is connected to the proper power supply. This arc generates some visible radiation, or light, but much more invisible ultraviolet energy, which excites fluorescent chemicals coated on the inside of the tube. Unlike the ordinary incandescent lamp, the goal of fluorescent lamps is not to produce a maximum of light directly but, rather, to generate efficiently short wave ultraviolet radiation and then to employ fluorescent chemicals or "phosphors" which can effectively convert that ultraviolet energy into visible light. A low pressure mercury arc produces an abundance of one particular wavelength in this short wave ultraviolet region, 2,537 angstroms, and phosphors are selected and blended to respond efficiently at that wavelength. Various phosphors are used to produce different colors of light.[1]

Of general artificial illuminants present use is confined almost exclusively to gas-filled (type C) tungsten filament incandescent lamps and to fluorescent lamps. The latter have various advantages and disadvantages and will be considered separately.

## PRINCIPLES OF APPLICATION

The ophthalmologist is most frequently requested to give advice as to the best kind of light and the intensities required. Such questions cannot be answered categorically, since the answers will vary with the person, the task to be performed and the surroundings.

The enumeration of five general principles may here prove helpful to the ophthalmologist when he is called on to evaluate a lighting system or to give advice regarding lighting.

*Intensity.*—A whole library might be filled with what has been written on the subject of levels of illumination, usually to the neglect of other factors, and the end has not been reached. Several catalogues of job analyses and their illumination requirements have been published by the Illuminating Engineering Society,[2] the American Institute of Architects and other national organizations.

In general, over the last fifty years there has been an upward trend in the recommended levels of illumination, particularly for work involving fine discrimination.

In 1896 Katz reported that 0.4 foot candle was the best average illumination when speed of reading was involved and argued that an illumination twenty-five times as intense as the threshold value was sufficient. Most authors up to 1912 recommended 2 to 4 foot candles as the optimum. In view of the lighting fixtures of those days, it is probable that the low intensities prescribed were conscious or unconscious attempts to eliminate excessive contrast or glare; moreover, light sources of high efficiency had not been developed.

Troland,[3] in 1931, after the most extensive review of the literature on this subject ever undertaken concluded:

1. Amick, C. M.: Fluorescent Lighting Manual, New York, McGraw-Hill Book Company, Inc., 1942.

2. Recommended Practice of School Lighting, New York, Illuminating Engineering Society, 1938; Recommended Practice of Office Lighting, ibid. 1939; Recommended Practice of Industrial Lighting, ibid., 1942.

3. Troland, L. T.: Analysis of the Literature Concerning the Dependency of Visual Functions on Illumination Intensity, Tr. Illum. Engin. Soc. **26**:107 (Feb.) 1931.

. . . the vast majority of industrial operations can be carried out at maximum efficiency with an illumination intensity in the neighborhood of 10 ft-c and many of these operations can be done equally well at 1 ft-c where contrasts and sizes of details to be perceived are not of threshold dimensions.

These conclusions were strongly opposed to numerous recommendations made in the past decade, chiefly by Luckiesh and his associates at the General Electric Corporation, who argued for levels fifty to one hundred times as high as those formerly considered optimum. The argument reached the lay press,[4] and charges were aired that the high recommendations were commercial propaganda.

The answer lies in the great range of adaptability of the human eye, which can function efficiently probably over a range of 10,000:1. It is unfortunate that so much publicity and emphasis have been given to this single factor of intensity. Ophthalmologists who are interested in getting details for a specific problem are advised to obtain a copy of the "American Recommended Practice of School Lighting" (or "American Recommended Practice of Industrial Lighting")[2] from the Illuminating Engineering Society. In these booklets high conservative levels are given for almost all tasks.

The effect of changes of illumination on ocular fatigue in the zones ordinarily encountered, that is, between 10 and 30 foot candles, is relatively unimportant. It is certain that continued use of the eyes, especially for fine work, under values of an order of 1 per cent of these intensities will result in eyestrain and functional inefficiency, with possible organic damage. A corresponding increase in these intensities to hundredfold values of artificial illumination will probably also result in eyestrain and ocular fatigue unless adjustment is made in the quality and distribution of the light.

*Quality.*—The quality, or spectral composition, of light is an important attribute so far as its effect on ocular efficiency and comfort is concerned. Most authorities agree that the more nearly the quality of the light approaches diffuse daylight, the better it is. In work involving color discrimination such spectral quality is essential. Tungsten filament light is relatively deficient in green, blue and violet radiation as compared with daylight. This invalidates it for color judgments, but for all ordinary purposes it serves well. Visual acuity is good under this light, and the preponderance of yellow radiations leaves it not unpleasing or uncomfortable to most people. There are some persons, however, who find themselves able to work longer and with less fatigue under artificial daylight. Both of us belong in this group, and we recommend artificial daylight for others so constituted. The units manufactured by the Macbeth Daylighting Company will be found satisfactory for persons who are comfortable when working or reading under daylight but who experience discomfort when using tungsten lamps. We know of no other commercial artificial daylight product of which this can be said. The "blue bulbs," so-called daylight bulbs, do not yield light of daylight quality, or even approach it. They represent perhaps a 15 per cent step in the direction from Mazda to north skylight. For the sake of precision, we should state the quality of our illumination in terms of one of the three internationally standardized illuminants—illuminants *A*, *B* and *C* of the International Commission on Illumination. The first, illuminant *A*, may be taken as a qualitative standard of tungsten filament light in units of 200 watts or above. Illuminant *B* may be taken as the qualitative standard for white light or sunlight of apparent color temperature near 5,000 K., and illuminant *C* is the standard for "daylight" lamps, approximating light overcast skylight of a color temperature between 6,500 and 7,000 K.

*Contrast.*—An important factor in evaluating or prescribing lighting is the contrast involved in the work being done. High contrast means increased visibility. Black on white can be discriminated very well under low illumination, whereas low contrast work requires more light. This is readily exemplified when one considers the relative visual work required to sew with black thread on black cloth and that involved in sewing with the same thread on white cloth. In the first instance a great increase in illumination is required to offset the disadvantage of low contrast. Contrast is frequently evaluated as per cent and fitted into lighting prescriptions on that basis.

For example, printing ink reflects little (approximately 4 per cent) of the light incident on it. Good white paper reflects about 80 per cent of the light incident on it. The contrast of such ink and paper, then, is 4 per cent on 80 per cent, or 76/80, which equals 95 per cent. If the ink reflects 8 per cent, the percentage contrast is 8 per cent on 80 per cent, or 72/80, which equals 90 per cent. In evaluating the illumination to be used in reading, the following illustration may be used: The material is printed in 8 point type, with an average blackness of

4. Light and Heat, Time **31**:30 (March 28) 1938.

8 per cent (reflectance). The paper has an 80 per cent reflectance. The brightness contrast is therefore 90 per cent. For such reading an illumination of 10 to 15 foot candles is recommended. This level should be increased if (1) the visual angle is smaller, as with 6 or 4 point type; (2) the contrast is less, as when the paper is old, yellowed, smudged or of poor quality; (3) speed and accuracy are needed, as in proof-reading; (4) the subject has poor eyes or a refractive error; (5) the subject has poor visual acuity with the best possible correction, or (6) the work requires prolonged periods of concentration. Good lighting in such a case increases visual efficiency, speed of seeing and comfort.

*Distribution.*—Distribution is an important factor in good lighting. Glare and its evil consequences, although a result of faulty distribution, will be considered separately. The distribution of light in the field of vision affects all the component visual functions, as well as the integrated act itself. However optimal other conditions may be, extreme variations in intensity occurring in the field of vision produce disturbing effects on the eye, and the disturbance is directly proportional to the size and intensity of the disturbing source and its proximity to the line of sight. Under certain conditions these extreme contrasts are desirable, as when an object near the threshold of acuity must be made visible, but in general pronounced and useless differences in brightness in the field of vision contribute to ocular inefficiency and the production of fatigue. This is especially true when the eye in its movements must subject the central portion of the retina to frequent and sudden changes in intensity of stimulus; the inability of the macula to meet these demands for repeated rapid adjustment results in temporary partial blindness—central scotoma. For greatest comfort the entire field of vision should be well and evenly illuminated, with perhaps a mild increase in the area of the working plane.

Unsteadiness of illumination is another source of fatigue, by producing incessant demands on the eye for readjustment. Under certain conditions, such as flicker, it is quickly and unpleasantly effective. Cloud or smoke shadows frequently cause rapid and annoying alterations in light values near windows.

Diffusion is related to distribution and shares its importance. Diffuse light does not cast sharp, dense shadows. As with contrast, under certain conditions these sharp shadows may add to visual efficiency, but these special conditions do not detract from the general statement that the more diffuse the light the better it is tolerated by the eye. Lancaster has characterized diffusion as an important quality of good lighting and has indicated a rough test for this quality: A pencil held a few inches from the paper, book or work to be viewed should not, and will not, cast a sharp shadow if the light is properly diffused.

*Glare.*—Glare is a factor in faulty distribution. Glare has been defined as useless light in the field of vision. Its importance increases as it approaches a position on the line of sight. Glare may be diffuse, specular or direct. Diffuse glare is the type experienced outdoors from too high intensities. Specular glare is the type produced by mirrors, highly polished metal and furniture, glossy paper and other shiny surfaces. Light specularly reflected from an object is not focused into an image on the retina. It is represented merely by a spot of unfocused light. If focused, it would form an image of the source of light, not of the reflecting object. However, in looking at an object one focuses for it, not for the source of light. Light diffusely reflected, since it begins its effective origin at the reflecting surface, forms an image alone of that surface on the retina. One thus sees objects only by diffusely reflected light. The light specularly reflected, since it forms an overlay of unfocused light on the image, blurs that image and is therefore not an aid, but a hindrance, to vision. There are three methods by which one may combat this type of glare: (1) The direction of the light may be changed; (2) the light may be completely diffused, or (3) specular reflection may be eliminated, partially at least, by Polaroid. Of the three methods, the first is the most practical and least expensive. Rhoads [5] gave a test for this type of glare: A fairly large mirror is placed on the working plane or where a book is to be held for reading. If any light sources can be seen in the mirror, then the working plane, the position of the body or the light source should be adjusted until the reflections disappear. Another method by which one may ameliorate, though not wholly avoid, such specular reflection is to make the light sources as extensive as feasible, thereby permitting a reduction in their intrinsic brilliance without reducing the illumination.

Direct glare arises from bright objects in the field of vision, such as headlights out of doors or unshaded lamps indoors. The unpleasant effects of such sources of glare are, as already stated, directly proportional to the brilliance of

5. Rhoads, J. N.: A Reflecting Book Marker for Teaching Readers How to Avoid Eye Strain, Ophth. Rec. **2**:416-419 (Aug.) 1913.

the object and its proximity to the line of sight, so that a 100 watt lamp 10 degrees from the line of sight will produce about as much glare as a 200 watt lamp 15 degrees from the line of sight. In order to avoid or reduce glare, the brilliance of light sources should be kept as low as possible. Reduction in the brilliance of the source will reduce the illumination unless compensation is made, and this compensation takes the form of increase in the area of the source. Hence large sources of low intrinsic brilliance, achieved through luminaire design, diffusing glasses or semi-indirect lighting, are distinctly preferable to small, bright sources (fig. 2). The whole evolution of lighting engineering in the past two decades has been in this direction. An excellent rule for one to follow in evaluating or prescribing such compensation is that the brightness of the

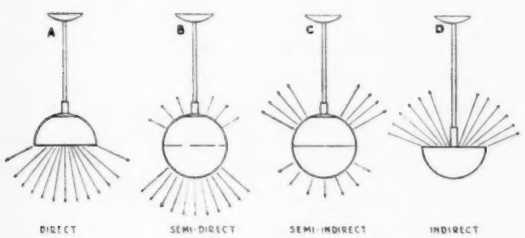


Fig. 2.—Types of lighting fixtures.

In this figure *A* shows direct lighting *B*, semidirect lighting; *C* semi-direct lighting and *D*, indirect lighting.

Three decades ago most lights had either no fixtures or were equipped with fixtures of type *A*. At present luminaires are preponderantly of type *C*.

source shall not be more than twenty (preferably ten) times the brightness of its background and, further, that the intrinsic brightness of the source shall not exceed 3 (preferably 1) candles per square inch.

A few rules of thumb suggestions may be helpful to one in evaluating or prescribing for an illumination situation:

1. The intensity of light, or the illumination level, is to be selected with reference to the patient and the nature of the work he is to do.

2. The quality is evaluated with reference to the task to be performed and the patient's preferences. Illuminant *C*, standardized by the International Commission on Illumination, is mandatory for most work involving color judgments and is preferred for general purposes by a large number of subjects.

3. The conditions of contrast have an important bearing on the intensity and quality recommended.

4. The distribution should be as even and diffuse as possible. Pronounced differences in brightness should be avoided. The Lancaster test for diffusion is helpful.

5. Glare is to be looked for and ameliorated or avoided. The Rhoads test for specular glare is helpful.

The background is to be kept diffusely illuminated. A good rule is that the ratio of illumination of the working plane to the background shall not exceed 4:1, and preferably should be less. The ratio of brightness of the source to that of the background should not exceed 20:1, preferably 10:1, and the intrinsic brilliance of the source should not exceed 3 (preferably 1) candles per square inch. In order to achieve an evenly diffuse illumination of 15 to 20 foot candles in a room with light walls and ceilings, there will be required (if a tungsten filament type C illuminant is used) about 2 to 3 watts per square foot of floor space. Higher general levels are rarely required and should not be recommended except under special circumstances, since the excessive infra-red radiations of such sources (90 per cent) would cause unpleasant heating in the summer time and might necessitate air conditioning.

## FLUORESCENT LIGHTING

The ophthalmologist will frequently be requested to give advice concerning the fluorescent tube lighting, introduced in 1938. This type of lighting has been growing in use and importance. In spite of six years of development, much is to be desired, and it is too early to give an unqualified opinion. It is obvious that one great fault has been inadequate design of fixtures to hold these tubes. The present period may be analogous to the middle teens, after the introduction of the gas-filled, unfrosted Mazda lamp. The present fluorescent tubes are too bright for comfort when unshielded, and most installations carry little or no shield. The intrinsic brightness of the 30 watt Mazda F lamp is 5.5 candles per square inch for the 3,500 degree white light tube and 4.5 candles per square inch for the daylight tube. All Mazda fluorescent tubes, except for the 14 and 15 watt types, have a brightness of over 3 candles per square inch.

When the lamp is used close to the work, as a desk lamp in the usual position at the back of the desk, the glare from specular reflection is pronounced. This fault is partially obviated if the lamp is placed along the side of the desk or table, on the left side for a right-handed person and on the right side for a left-handed person.

The advantages of the fluorescent tubes are their high lumen per watt efficiency and the flexibility, within a limited range, with which their color value can be changed.

They do not, however, and probably cannot be made to, give the spectral curve of daylight, and time and experience are necessary to show whether deviations in this respect are deleterious. The fluorescent tubes are best suited for installations in large areas and are particularly useful in air-conditioned interiors because of their relatively low heat ouput. They should always be mounted high. Their recommendation for small rooms in the present state of development of the lamps and fixtures is questionable.

Many people, sensitive and insensitive, work happily, efficiently and comfortably under fluorescent lighting. Many others, and they are not neurotic or reactionary persons incapable of absorbing new ideas, have experienced discomfort and great unpleasantness since the installation of fluorescent lighting. Common complaints are ocular fatigue, burning of the eyes, headache, tearing and a feeling of sand in the eyes.

At the Knapp Memorial Laboratories, where studies on fluorescent lighting have been carried out, we have been inclined to explain the unpleasant effects of this type of lighting in terms of six factors: (1) flicker, either (*a*) total or (*b*) electrode; (2) spectral quality; (3) high intrinsic brightness; (4) radiation of wavelength of 312 to 313 millimicrons; (5) lag of emission in the blue-green-yellow portion of the spectrum, and (6) stroboscopic effect.

The total flicker is usually due to insufficient voltage or to deteriorated lamps, although electrode flicker has frequently been seen when neither of these factors was apparently present. The spectral quality, we are sure, affects color vision and may produce unpleasant psychologic effects. Probably the chief difficulty arises from the high intrinsic brightness, which varies from 5.5 candles per square inch, in the 30 watt white light tube, to 3.3 candles per square inch, in the 40 watt daylight tube. We strongly believe that intrinsic brightness should be kept below 3, preferably 2, or even 1, candles per square inch. We feel sure that diffusing covers for fluorescent tubes will be used more and more in the future.

Fluorescent tubes emit a fairly strong double line at 312 to 313 millimicrons. Some of this radiation may pass through the glass of the tube. Quantitative measurements are at present under way to evaluate this factor, which may prove to be important. Ultraviolet radiation of this wavelength might have two effects. Such rays are abiotically active, and since the effect of such radiation is cumulative, prolonged exposure might result in irritation of the cornea and conjunctiva. Another, and so far unconsidered, effect is the intraocular fluorescence which might be produced if this radiation reaches the lens of the eye; in this case the overwash of fluorescent light generated within the eye might be very unpleasant.

The lag of emission of the blue-green-yellow components from a fluorescent tube results from the difference in excitation periods of the various phosphors used in coating the tube and may easily be demonstrated by observing such a tube in action through a stroboscope. There is a large, brief, blue peak, followed by other component colors. Whether this "blue beat," or the lag of emission of the other colors, has any visual, physiologic or psychologic significance is not yet known.

Finally, the well known stroboscopic effect of fluorescent lights makes them unpleasant for the illumination of rapidly moving machine parts. This effect can be partly overcome by use of multiple, out of phase tubes, but the best ratio so far achieved has been 3 to 1 (a Mazda incandescent lamp being used as 1). Fluorescent lighting should not yet completely displace the more conventional types.

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# ANALYSIS OF CASES OF ANISEIKONIA

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The doubts enumerated in an editorial by Crisp [1] suggested the following presentation of and comments on cases of aniseikonia.

The patients who come for examination for aniseikonia have been well described by Post.[2]

> [They are] only those whom he [the ophthalmologist] has failed to relieve with the usual lenses . . . and who, in general, . . . are bothered by ocular as well as other trivialities and often have exhausted his patience. Thus, the aniseikonic clinics have become the rendezvous of the most difficult patients for whom to obtain comfort. That *anything* good is accomplished for these patients is the miracle.

Crisp's first question was how large a proportion of the ocular difficulties apparently relieved by prescription for aniseikonia were capable of relief in no other way, and, second, what proportion could have been relieved by more complete accuracy in refractive measurements without the aid of size lenses.

Since September 1942 I have made the examinations for aniseikonia of the patients referred to the department of ophthmalology of the Northwestern University Medical School. One hundred and seventeen examinations have been made (table 1), and of this number 97 examinations were complete enough to allow for analysis. Sixty-one patients showed an appreciable amount of aniseikonia; 17 showed no aniseikonia, and 19 had such poor fusion that examination was impossible until after some form of muscle training.

TABLE 1.—*Data on Patients with Aniseikonia*

| | |
|---|---|
| Patients with aniseikonia | |
| Comfort with iseikonic lenses | 14 |
| Improvement with iseikonic lenses | 3 |
| No improvement with iseikonic lenses | 4 |
| Reading difficulties | 3 |
| Patients reexamined | 20 |
| Patients with no aniseikonia | 17 |
| Patients with poor fusion | 19 |

Iseikonic lenses were ordered for 24 patients, and of this number 14 stated that they had obtained complete comfort, with disappearance of their asthenopic symptoms. Three reported that the condition was improved, and 4 noticed no improvement.

TABLE 2.—*Data on Three Patients with Reading Difficulties Given Iseikonic Lenses*

| Name | Age, Yr. | Improvement | Prescription | Comment |
|---|---|---|---|---|
| B | 17 | + | (R) +2.50 D. sph. ⊃ −0.50 D. cyl., ax 165; vision 20/16<br>(L) + 2.50 D. sph. ⊃ −0.50 D. cyl., ax 15 ⊃ 0.50% over-all magnification ⊃ 1.50% meridional magnification, ax 90 (vision 20/16)<br>September 1942 | Divergence insufficiency; reading ability improved; no symptoms of asthenopia |
| N | 10 | + | (R) −0.75 D. sph. ⊃ 0.75% over-all magnification (vision 20/20)<br>(L) −0.50 D. sph. (vision 20/20)<br>November 1943 | Considerable improvement the first two months. Patient did better later, but performance not up to average or to his intelligence quotient |
| M | 16 | + | (R) +2.75 D. sph. ⊃ −0.75 D. cyl., ax 25 ⊃ 1.5 △ (vision 20/13-2)<br>(L) +2.50 D. sph. ⊃ −0.75 D. cyl., ax 150 ⊃ 1% meridional magnification, ax 180 (vision 20/15)<br>September 1941 | Convergence insufficiency; alternate macular suppression. September 1943: Aniseikonia unchanged; reading ability improved, with correction of muscle balance |

Of this number, 3 students, aged from 10 to 17, who had reading difficulties were given iseikonic lenses after a complete general study and remedial reading efforts had given little help (table 2). The 3 patients showed some improvement immediately after use of the lenses. The high school student in his last year, as a senior, did the best work of his twelve years in school but continued to find reading a slow process. The other high school student, in her first year, im-

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1. Crisp, W. H.: Aniseikonia Doubts, editorial, Am. J. Ophth. **26**:1329 (Dec.) 1943.

2. Post, L. T.: Future of Aniseikonia, editorial, Am. J. Ophth. **26**:321 (March) 1943.

proved much more rapidly after the convergence insufficiency was corrected with the use of loose prisms. The 10 year old boy is not progressing as his mental rating indicates that he should.

Thirteen of the 14 patients who were comfortable with the correction of the size difference had worn the same refractive corrections without comfort for several weeks to several months prior to their being fitted with the iseikonic lenses. Data on 4 of them are shown in table 3. Three of them had a convergence insufficiency which was improved by the use of loose prisms before the iseikonic lenses were ordered (table 4).

The teacher aged 30, was not comfortable with the iseikonic lenses until the convergence was improved. The judge, aged 58 (table 5), who was one of the most interesting patients, had never been able to use his eyes with any comfort since he was in high school and had been much more uncomfortable after reading glasses were necessary. Vision in the left eye was poor, and an area of macular suppression was outlined by the mirror screen test. Vision in this eye improved to 20/50 with macular stimulation and occlusion of the right eye. At this time a satisfactory examination for aniseikonia was made, and a total size difference of 3.5 per cent in the 90 degree meridian was found for the left eye. This correction was ordered as a temporary fit-over lens; the patient had great relief immediately

TABLE 3.—*Data on Four Patients Who Were Comfortable with Iseikonic Lenses*

| Name | Age, Yr. | Occupation | Muscle Balance | Prescription | Comment |
|---|---|---|---|---|---|
| A | 34 | Proofreader | Normal limits | (R) —1.25 D. sph. ⊃ —0.37 D. cyl., ax 15 (vision 20/13)<br>(L) —2.75 D. sph. ⊃ —0.25 D. cyl., ax 180 ⊃ 1.25% over-all magnification ⊃ 1.50% meridional magnification, ax 90 (vision 20/13)<br>March 1943 | Ocular discomfort began as myopia developed while patient was in college |
| B | 59 | Physician | Right hyperphoria | (R) +1.50 D. sph. ⊃ +1.50 D. cyl., ax 95 ⊃ 1.25% over-all magnification ⊃ 0.50% meridional magnification, ax 180 (vision 20/16)<br>(L) +2.25 D. sph. ⊃ +0.50 D. cyl., ax 125 (= vision 20/16 +2.00<br>September 1942 | First time lenses were worn patient could read with comfort for hours (patient died 1943) |
| B | 30 | Teacher | Convergence insufficiency | (R) —1.00 D. sph., ax 95 ⊃ 2.5% meridional magnification, ax 90 (vision 20/16)<br>(L) —1.00 D. sph., ax 80 (vision 20/16) | Eyes became comfortable as convergence insufficiency improved |
| G | 45 | Cartographer | Normal limits | (R) —1.00 D. sph. ⊃ —2.00 D. cyl., ax 90 ⊃ 2% meridional magnification, ax 90 (vision 20/13)<br>(L) —1.50 D. sph. ⊃ —2.00 D. cyl., ax 65 ⊃ 0.25% meridional magnification, ax 180 (vision 20/13) | Car sickness has disappeared; "glasses are wonderful" |

TABLE 4.—*Data on Patients Who Were Comfortable with Iseikonic Lenses*

| Name | Age, Yr. | Occupation | Muscle Balance | Prescription | Comment |
|---|---|---|---|---|---|
| H | 30 | Business manager | Convergence insufficiency | (R) —0.50 D. sph., ax 165 ⊃ 1.25% meridional magnification, ax 90 (vision 20/16)<br>(L) —0.50 D. sph., ax 15 (vision 20/16)<br>January 1944 | Exercises with loose prisms until convergence for near vision = 100 △ base out was perfectly comfortable |
| L | 10 | School boy | Normal limits | (R) +3.50 D. sph. ⊃ —4.25 D. cyl., ax 7 ⊃ 2.5% meridional magnification, ax 180 (vision 20/30+)<br>(L) +0.25 D. sph. ⊃ —0.25 D. cyl., ax 180 ⊃ 3% meridional magnification, ax 90 (vision 20/20+)<br>March 1944 | Patient has worn iseikonic lenses four years with comfort; anisometropia (patient needed larger frames) |
| L | 45 | Business | Convergence insufficiency | (R) —1.12 D. sph. ⊃ 3.0 △ base out (vision 20/16)<br>(L) —1.12 D. sph. ⊃ —0.50 D. cyl., ax 90 ⊃ 3.0 △ base out ⊃ 1.75% meridional magnification, ax 90 (vision 20/16)<br>September 1942 | June 1943: lenses comfortable for distance; patient wants reading pair |
| O | 28 | Lieutenant in Navy | Normal limits | (R) +0.50 D. sph. ⊃ —1.00 D. cyl., ax 5 (vision 20/13)<br>(L) +1.00 D. sph. ⊃ —1.00 D. cyl., ax 180 ⊃ 1.5% over-all magnification (vision 20/13)<br>October 1942 | Prescription worn previously without magnification |
| R | 31 | Lieutenant in Navy | Convergence insufficiency | (R) —0.37 D. sph. ⊃ —0.75 D. cyl., ax 60 (vision 20/16)<br>(L) —0.37 D. sph. ⊃ —0.75 D. cyl., ax 155 ⊃ 1% over-all magnification (vision 20/16)<br>December 1942 | Reading time now unlimited; prescription worn previously without magnification |

and wanted permanent lenses made. Vision continued to improve in the left eye. As he had an oblique astigmatism he was advised to have an examination at the Dartmouth Institute, since he was going East, in order to have the measurements checked by the space eikonometer. The readings at the institute were practically the same, and the permanent lenses were ordered with 2.5 per cent magnification, axis 90.

The patients who had only improvement (table 6) all had convergence insufficiency. In the case of H. the results of the first examination, in March 1943, were satisfactory, and no outstanding muscle imbalance was found with the eikonometer, although she had worn glasses with vertical prisms previously. She wore the iseikonic lenses with great comfort for five months; then the asthenopic symptoms recurred. Examination at this time showed alternate macular suppression and poor amplitude. As the fusion and the amplitude improved, the asthenopic symptoms largely disappeared, and she has been able to take off the iseikonic glasses except for reading.

TABLE 5.—*Data on Patients Made Comfortable with Iseikonic Lenses*

| Name | Age, Yr. | Occupation | Muscle Balance | Prescription | Comment |
|---|---|---|---|---|---|
| P | 28 | Accountant | Convergence insufficiency | (R) +0.75 D. sph. ⊃ −0.25 D. cyl., ax 180 ⊃ 2 △ base in (vision 20/16)<br>(L) +0.75 D. sph. ⊃ −0.25 D. cyl., ax 180 ⊃ 2 △ base in ⊃ 3% meridional magnification, ax 90 (vision 20/16)<br>November 1942 | Previous prescription same without base-in prisms and magnification |
| P | 34 | Lithographer | Right hyperphoria 3 | (R) −2.62 D. sph. ⊃ −0.62 D. cyl., ax 160 ⊃ 1.25 △ base down ⊃ 0.75% meridional magnification, ax 90 (vision 20/16)<br>(L) −3.00 D. sph. ⊃ −2.25 D. cyl., ax 172 ⊃ 1.25 △ base up ⊃ 1.75% meridional magnification, ax 180 (vision 20/16)<br>September 1942 | Eyes had never been comfortable from age of 10 until iseikonic lenses were prescribed in 1939 at Washington University |
| S | 48 | Salesman | Normal limits | (R) +4.00 D. sph. ⊃ −0.50 D. cyl., ax 105 (vision 20/16)<br>(L) +1.25 D. sph. ⊃ 2% over-all magnification (vision 20/16); +1.50 D. sph. added<br>August 1943 | Eyes never uncomfortable until glasses were needed |
| W | 65 | Lawyer | Left hyperphoria 3 | (R) −3.00 D. sph. ⊃ −0.25 D. cyl., ax 180 ⊃ 0.50% over-all magnification ⊃ 2.25% meridional magnification, ax 180 (vision 20/16)<br>(L) −2.00 D. sph. ⊃ −0.50 D. cyl., ax 90 ⊃ 2 △ base down (vision 20/16); +2.25 D. sph. added<br>August 1943 | Prescription without magnification helped some, but patient has had complete relief with iseikonic lenses |
| S | 58 | Judge | Amblyopia with left macular suppression | (R) +1.25 D. sph. ⊃ −0.25 D. cyl., ax 75 ⊃ 1.25% meridional magnification, ax 180 (vision 20/16)<br>(L) +3.50 D. sph. ⊃ −1.00 D. cyl., ax 80 ⊃ 1.50% meridional magnification, ax 90 (vision 20/33); +2.00 D. sph. added<br>February 1944 | Left eye: Vision before macular stimulation 20/100; with iseikonic lenses, 20/33 |

TABLE 6.—*Data on Patients Whose Vision Was Improved with Iseikonic Lenses*

| Name | Age, Yr. | Occupation | Muscle Balance | Prescription | Comment |
|---|---|---|---|---|---|
| D | 53 | Housewife | Convergence insufficiency | (R) +2.00 D. sph. ⊃ −0.25 D. cyl., ax 120 ⊃ 0.50 △ base up ⊃ 2% meridional magnification, ax 180 (vision 20/20)<br>(L) +2.25 D. sph. ⊃ −0.25 D. cyl., ax 90 (vision 20/20); +2.25 D. sph. added<br>January 1943 | Patient had first pair of glasses in January 1942; second examination January 1943; patient can read for only an hour with comfort; lenses comfortable for distance |
| H | 43 | Housewife | Convergence insufficiency; alternate macular suppression | (R) +1.00 D. sph. ⊃ −0.75 D. cyl., ax 90 (vision 20/16)<br>(L) +1.00 D. sph. ⊃ 1.25% meridional magnification, ax 180 (vision 20/16); +1.25 D. sph. added<br>April 1943 | As convergence insufficiency and binocular fusion improved, eyes were comfortable |
| W | 40 | Dentist | Convergence insufficiency | (R) −0.50 D. sph. ⊃ −1.25 D. cyl., ax 110 ⊃ 0.25% over-all magnification ⊃ 0.50% meridional magnification, ax 90 (vision 20/16)<br>(L) −0.50 D. sph. ⊃ −1.25 D. cyl., ax 90 (vision 20/16); +1.00 D. sph. added | Some remaining fatigue, but patient can use eyes now for several hours at the chair |

For the patients who received no help from the iseikonic lens (table 7) there was no satisfactory explanation. Two of them showed some muscular imbalance with the eikonometer; the other 2 did not.

Twenty patients who came for reexamination had been wearing iseikonic lenses from one to seven years. Seven who were uncomfortable had poor muscle balance, poor amplitude with macu-

lar suppression or convergence insufficiency. Two of these 7 patients were able to take off their glasses except for reading when the muscle balance was improved. Two had associated glandular dyscrasia, and the glasses were discarded after specific medication. The measurements of the size difference of the images was found to be practically the same for all patients as the values obtained at the previous examinations.

The 19 patients for whom the examination was entirely unsatisfactory had poor binocular vision, which included poor fusion with suppression, poor amplitude, divergence insufficiency or convergence insufficiency. These patients were instructed to return for reexaminations after improvement of the muscle balance.

careful refractive corrections first is answered by the results with the patients who were made comfortable with the iseikonic lenses, since the majority of these patients had worn the same prescription for their refractive correction before size magnification was added; it is to be pointed out, also, that their muscle balance was normal or was restored to normal with simple treatment.

In answer to the second question, as to what proportion of ocular disturbances could have been relieved by greater accuracy in refractive measurements without the aid of size lenses, the corrected vision of the patients was excellent as a rule, and the refractive measurements were usually accepted; but the ocular muscle balance was frequently inadequate, and a satisfactory examination for aniseikonia was not possible until

TABLE 7.—*Data on Patients Who Were Uncomfortable with Iseikonic Lenses*

| Name | Age, Yr. | Occupation | Muscle Balance | Prescription | Comment |
|---|---|---|---|---|---|
| E | 52 | Salesman | Left hyperphoria 1 | (R) −0.50 D. sph. ⊃ −0.50 D. cyl., ax 145 ⊃ 1 △ base up (vision 20/16<br>(L) −1.25 D. sph. ⊃ −0.50 D. cyl., ax 180 ⊃ 1.5% meridional magnification, ax 180 (vision 20/16)<br>April 1942 | Eyes comfortable for short period after adjustment of eye wire distance; same glasses previously without magnification |
| F | 44 | Housewife | Convergence insufficiency | (R) +1.00 D. sph. ⊃ −0.25 D. cyl., ax 30 ⊃ 0.75% over-all magnification (vision (20/20)<br>(L) +1.25 D. sph. ⊃ −0.50 D. cyl., ax 150 (vision 20/16); +1.50 D. sph. added<br>February 1943 | Glasses for distance comfortable; reading glasses no help |
| G | 61 | Housewife | Normal | (R) +2.00 D. sph. ⊃ −0.50 D. cyl., ax 180 ⊃ 2% meridional magnification, ax 90 (vision 20/16)<br>(L) +2.25 D. sph. ⊃ −0.50 D. cyl., ax 175 ⊃ (for reading) +1.75% magnification<br>June 1943 | Glasses good only for objects at arm's length; discarded after two weeks |
| M | 47 | Office work | Normal | (R) +3.00 D. sph. ⊃ 4% meridional magnification, ax 90<br>(L) +2.00 D. sph. (Jaeger test type 4)<br>June 1943 | Reading glasses only |

Some of the remaining 17 patients who had aniseikonia of varying amounts had symptoms which indicated a general disturbance, and they were advised to return after this condition had received attention. Two patients would not order the glasses for cosmetic reasons, and some patients are receiving muscle training.

Any patient with an oblique astigmatism and a size difference should be tested with the space eikonometer, as this adaptation is not available for the standard eikonometer; this may account for failure in some cases.

## COMMENT

The answer to Crisp's question of how large a proportion of the ocular difficulties apparently relieved by prescriptions for aniseikonia could have been relieved if the patients had worn the binocular fusion was improved and until it could be maintained. With improvement in the maintenance of binocular fusion, several of the patients were as comfortable without the glasses as with them.

It was also notable that many of the patients had never had any particular ocular discomfort until vision was improved with glasses, especially at the age of presbyopia, when it became necessary for them to wear glasses. Then improved vision, with the binocular attempts, brought out asthenopic symptoms.

In conclusion, binocular fusion and ocular muscle balance, together with refraction and size magnification should be considered of basic importance, for the comfortable use of the eyes as the "seeing organ."

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# UNUSUAL FORMS OF NYSTAGMUS

## WITH A REVIEW OF THE LITERATURE

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The purpose of this article is to discuss several unusual and comparatively rare forms of nystagmus which we have seen and to present a detailed report of a case. Two types of ocular nystagmus, volitional and occupational, and a form of mixed nystagmus due to compression of the upper cervical portion of the cord, are considered.

Fundamentally, nystagmus may be of vestibular, cerebellar, cerebral, upper cervical or ocular origin. The optic system is involved in all forms, but it is only in the ocular type that it is directly affected. In all other cases it is involved indirectly by way of the vestibular system. The vestibular system may be the seat of origin of irritative phenomena and transmit the abnormal impulses to the ocular system, or the pathologic change may be in the cerebrum, the cerebellum or the upper cervical portion of the cord, in which event the vestibular system, together with the posterior longitudinal fasciculus, acts as a nucleus for the mediation of the abnormal impulses.

### REPORT OF CASES

CASE 1.—*Mixed nystagmus, secondary to compression of the upper cervical portion of the cord.*

A young soldier was admitted to the orthopedic section of the Walter Reed General Hospital, Washington, D. C., in the fall of 1941, with a compressed fracture of the body of the third cervical vertebra and mild involvement of the spinal cord. Reduction was successfully carried out, and halter traction was applied. The patient remained well for about four weeks; then occipital headache developed, and he complained of constant motion of objects with fixation of the eyes and slight numbness of the upper extremities. Neurologic examination revealed nothing significant except for a slight degree of hypesthesia, incomplete, in both arms and notable bilateral rotary nystagmus on direct gaze, in accommodation both for the near and for the far point. On lateral gaze, the rotary nystagmus disappeared and was replaced by bilateral horizontal nystagmus, the quick component being in the direction of gaze. The signs were interpreted as due to compression of the spinocerebellar pathways. Roentgenograms showed fairly good reduction of the fracture, although there was slight displacement. Further manipulation and traction were performed, and the symptoms finally disappeared. The patient had an uneventful convalescence.

CASE 2.—*Volitional nystagmus.*

A young private was admitted to a general Army hospital in the winter of 1943, complaining of weakness and stiffness of the muscles of the legs and arms. When, in the course of routine neurologic examination, the patient was requested to follow a cotton applicator with his eyes, he promptly volunteered that he could at will move his eyes back and forth at a very fast rate, and he seemed proud of the fact. When he was asked to demonstrate this phenomenon, he promptly produced a bilateral horizontal nystagmus, of pendular type, fast rate and large amplitude. He stated that he could keep up the motion for an indefinite period were it not that after fifteen or twenty seconds he became light headed and his eyes became tired. Another case of volitional nystagmus has been seen by one of us (H. C. S.).

CASE 3.—*Occupational nystagmus.*

A sergeant aged 28, white, a draftsman, was admitted to an Army station hospital on Sept. 1, 1943, with the complaint of blurring of vision and a sensation of jumping of objects in the horizontal plane. He was transferred to an Army general hospital on September 10, with the diagnosis of severe bilateral horizontal nystagmus, of undetermined cause. Vision was 20/50 in the right eye and 20/50 in the left eye.

*History.*—The patient was inducted into the Army on July 12, 1940. Vision at that time was 20/30 in each eye, and he had no complaints referable to the eyes. The past and family histories were without significance. Two months after induction the patient commenced work as a map plotter, doing a considerable amount of close work which involved plotting and triangulation.

*Present Illness.*—The first symptoms appeared in March 1941, approximately six months after the map work was begun. After about five hours of work he experienced a sensation of drawing and aching in the region of the supraorbital ridges, accompanied by slight blurring of vision and the sensation of jumping of objects in the horizontal plane. The duration of these attacks was ten to fifteen minutes. A brief rest was followed by relief, and work could be resumed. During the course of the next few months the attacks became more frequent, and a longer period of rest was required before the symptoms disappeared. Finally, however, the periods of rest gave only partial relief, and by June 1941 the patient was forced to do only part time work. Vision at that time was 20/50 in each eye.

During the course of the next two years the patient continued to work with maps as a part time job, and he noted that prolonged use of the eyes greatly aggravated the blurring of vision and the sensation of jumpiness of objects. Rest afforded some relief, although more or less permanent blurring and the sensation of to and fro motion of objects persisted. Vision in February 1943 was 20/100. At that time, however, he was doing class work at school in addition to the map work and was using his eyes constantly.

He continued to work until the time of his admission to the hospital. No progression or remission of symptoms had been observed in the six months prior to his admission.

*Examination.*—Physical examination, including a complete ophthalmologic and neurologic study, revealed nothing abnormal except for the ocular condition. Vision was 20/50 in the right eye, with ability to read Jaeger test type 1, and 20/50 — 1 in the left eye, with ability to read Jaeger test type 2, and was uncorrectable. The fields of vision were normal.

External examination revealed a moderate degree of horizontal nystagmus. The pupillary reactions were normal, and the pupils were round and equal on the two sides. The transparent media were normal. Slight blurring of the nasal sides of the optic disks was present, but this appeared to be within normal limits. The tentative diagnosis was nystagmus of ocular type, not associated with a neurologic condition. This opinion was confirmed by repeated careful neurologic examinations. The oscillation of the eyeballs was in the horizontal direction, and the components of the nystagmus were of equal rate and amplitude, so that a pendular type of motion resulted. Lateral gaze produced slight exaggeration of the rate but did not affect the amplitude. The nystagmus was not influenced by accommodation. There was no indication that the condition was of vestibular (labyrinthine), cerebellar or cerebral origin.

The diagnosis was severe bilateral horizontal nystagmus, of ocular type and occupational origin.

## COMMENT

The occurrence of nystagmus with lesions of the cord is uncommon. A review of the literature, however, indicates that a number of cases have been reported. It is assumed that in case 1 the nystagmus was the result of interference with the spinocerebellar pathways, resulting in abnormal stimulation of the cerebellum, which, in turn, involved the optic system. Oppenheim [1] stated that nystagmus may occur in cases of involvement of the spinal cord.

About 12 cases of volitional nystagmus have been reported in the literature. The nystagmus was of the horizontal type. Rea [2] stated that voluntary nystagmus has been described by Pyle and Ball and others. Cases of both the unilateral and the bilateral form have been reported. Persons with voluntary nystagmus have never had true nystagmus. According to Bing,[3] nystagmus not infrequently occurs in cases of hysteria, and nystagmus may be produced voluntarily by the hysterical person. Hysterical nystagmus, unlike the oscillating nystagmus caused by an organic lesion, is jerky and irregular.

With 3 exceptions, miners' nystagmus excluded, a review of the literature of the past twenty-five years failed to reveal any case of occupational nystagmus. Fuchs [4] referred to the occurrence of nystagmus in compositors, which he ascribed to a strained position of the eyes. Wilson [5] reported cases of nystagmus occurring in train dispatchers and crane workers. McCord [6] gave an excellent description of occupational nystagmus in train dispatchers. He reported 81 cases, in all of which the nystagmus was of the horizontal type. The condition is accepted to be of occupational origin and is attributed to continual motion of the large train sheet beneath the eyes and the movement of the head and eyes over the train sheet, both necessary in the continual recording of data concerned with movements of trains. McCord also stated that among jewelers, draftsmen, compositors and persons doing similar close work nystagmus had occasionally been encountered. (In 1 instance a train dispatcher who had not followed his occupation for eight years was observed still to exhibit nystagmus.) McCord [6] also stated that while it requires fifteen to twenty years for miners' nystagmus to develop, the other forms of occupational nystagmus may appear after as little as one year of work at the particular trade. These forms of occupational nystagmus are not as severe or incapacitating as is miners' nystagmus.

The pathophysiology and the pathogenesis of occupational nystagmus are the result of the interaction of several factors: namely, poor and improper illumination; the mechanical to and fro movement of the eyes incident to the particular occupation, and retinal fatigue. Adequate illumination is important in that the strain is relieved and the factor of retinal fatigue is minimized. This is the all-important factor in miners' nystagmus, so much so that the condition is practically nonexistent when miners are provided with proper illumination. The mechanical factor (the to and fro movements) may be interpreted as a coordinated and purposeful act primarily provoked by an external stimulus which is of the nature of an occupation requiring synchronized ocular activity. Constant repetition leads to habitual and involuntary reproduction

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of the act, which for no other purpose assumes the nature of an irrepressible impulse. Both inopportune and excessive, the act develops into a habit spasm, or tic, so that what started to be a physiologic adaptive process actually resolves into a pathologic condition. The added factor of retinal fatigue facilitates the establishment of the habit, so that a dilemma is presented. In this respect nystagmus may be looked on as a compensatory mechanism incited by an attempt at avoidance of retinal fatigue by engaging more retinal elements in the visual effort and protecting other retinal elements. Casten [7] stated the belief that nystagmus possibly results from the attempt at stimulation of more retinal elements in order to improve vision and stressed the importance of change of occupation, which he felt to be imperative. Mackie [8] stated that nystagmus is unknown in India, where the miners alternate mining with agriculture. He expressed the opinion that nystagmus is a physiologic adaptation, but with potential risks in the event of loss of control. Krieg [9] pointed out that the disturbance of the optic system which produces nystagmus may be due to lack of development of the macula, very poor vision, dim light or visual fatigue. All these conditions dispose to inability to fix the macula on a point. The two components of ocular nystagmus are usually of uniform rate; i. e., the slow and the rapid component lack differentiation. Rea,[2] in discussing macular function, stated that nystagmus was a physiologic adaptation in an effort at the prevention of fatigue. Citing Healy, he stated: "At first the oscillations are a physiological psycho-optical reflex; they become eventually a pathological habit-spasm." Bing [3] suggested that since optic nystagmus occurs in persons who are amblyopic, the afferent arc through which the altered impulses are propagated may be the proprioceptive fibers, originating in the extraocular muscles, and not the optic nerve. With defective conditions of the retina, the nystagmus is brought about by the patient's straining the muscles in order to obtain a better definition of the object. Such conditions include albinism; loss of macular rods occurring in persons, such as miners, who work in dim light, and various other conditions producing blindness. This type of nystagmus may be an ocular device to "spread" the image over more rods and cones and thus to obtain better vision.

7. Casten, V. G., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, chap. 52, p. 968.

8. Mackie, E. S.: Miners' Nystagmus, Brit. M. J. 2:258 (Aug. 1) 1936.

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# DIBUTOLINE SULFATE

## A NEW MYDRIATIC AND CYCLOPLEGIC DRUG

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IOWA CITY

There has been need in ophthalmology for new mydriatic and cycloplegic drugs. Hypersensitivity and idiosyncrasies to atropine and its derivatives are not uncommon. Also, the dosage of the more potent members of the group is limited by undesirable systemic effects, e. g., excitation and depression of the central nervous system, flushed face and drying of secretions. Finally, the ocular effects of atropine and scopolamine are unduly prolonged and are not readily counteracted. Recently we have synthesized the first substitutes for the atropine series effective on the eye.[1] The new mydriatic and cycloplegic drugs are surface active carbamic acid esters of the choline type and, therefore, are chemically unrelated to atropine. The ocular effects of the first of the new class of drugs have been reported previously.[2] Herein are described the ocular pharmacologic effects and some clinical applications of dibutoline, a name for the latest and most effective member of the series.

Dibutoline sulfate (dibutylcarbamate of dimethylethyl-$\beta$-hydroxyethyl ammonium sulfate) is chemically related (fig. 1) to carbaminoylcholine chloride but has different physical properties and antagonistic pharmacologic effects on the intraocular muscles; i. e., dibutoline is surface active and mydriatic, while carbaminoylcholine is surface inactive and miotic. Sulfate salts of dibutoline occur as white crystals which readily dissolve in water to form a clear, colorless solution with a slightly bitter taste and a faintly aromatic odor. Heat and light result in slow decomposition, but the solutions are stable at room temperature for weeks. Partially decomposed solutions become less potent, but the decomposition products are not toxic. The new drug is not an alkaloid and therefore does not have the considerable chemical incompatibilities of atropine.

Dibutoline sulfate should be dissolved in distilled water. In a saline or buffer solution dibutoline forms salts, e. g., dibutoline chloride, which are considerably more surface active than the sulfate and therefore more likely to cause

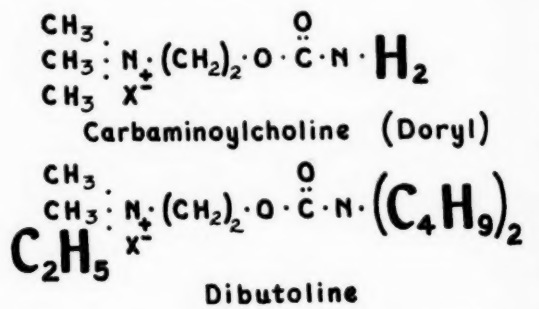


Fig. 1.—Formula for carbaminoylcholine chloride and dibutoline sulfate.

conjunctival irritation. A solution of 5 per cent dibutoline sulfate in distilled water is nearly neutral ($p_H$ 6.5), is of almost the same osmotic pressure as isotonic solution of sodium chloride and has an air-water interfacial tension of 47 to 48 dynes per cubic centimeter at 25 C.

Dibutoline produces paresis of smooth muscles innervated by the parasympathetic nervous system. Its effects on the smooth muscles of the eye, therefore, simulate those of paralysis of the oculomotor nerve; i. e., dibutoline produces paresis of the sphincter of the iris and the ciliary muscles. The action of dibutoline on the intraocular muscles is antagonistic to that of pilocarpine, physostigmine, acetylcholine and carbaminoylcholine.

Dibutoline has no effect on the ocular muscles innervated by the sympathetic nervous system, i. e., the smooth muscle of the lid and the dilator

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1. Swan, K. C., and White, N. G.: Some New Choline Esters with Cycloplegic and Mydriatic Action, Proc. Soc. Exper. Biol. & Med. **53**:164-166 (July) 1943.

2. Swan, K. C., and White, N. G.: (*a*) Choline Esters with Atropine-Like Action, J. Pharmacol. & Exper. Therap. **80**:285-288 (March) 1944; (*b*) Di-N-Butyl-Carbaminoylcholine Sulfate: A New Mydriatic and Cycloplegic Drug, Arch. Ophth. **31**:289-291 (April) 1944.

fibers of the iris. It does not produce widening of the palpebral fissure, which is effected by epinephrine, cocaine and related compounds; neither does it significantly alter reactivity of the dilator fibers of the iris to electrical stimulation of the cervical sympathetic nerve or to stimulatory drugs. Mydriasis produced by the new drug, therefore, may be enhanced by administration of epinephrine or related compounds, which act by stimulating the dilator fibers.

The relative potency of dibutoline sulfate and of homatropine hydrobromide was studied on the iris of the albino rabbit. Intravenous injections of 1 per cent solutions of the drugs were made in 10 animals to determine the minimal dose of each drug producing dilation of the pupil and loss of the light reflex. Two to 5 mg. per kilogram of body weight of each of the two drugs injected intravenously usually produced an immediate increase of 4 to 5 mm. in the horizontal diameter of the pupil, while injection of 10 mg. per kilogram of body weight resulted in total loss of the pupillary reaction to light. No synergism between the two drugs was demonstrated; i. e., 5 mg. of each of the two drugs injected simultaneously had approximately the same effect as 10 mg. of either drug injected separately.

Although when they were given by intravenous injection homatropine and dibutoline were of equal potency, when the two drugs were given by instillation dibutoline was more effective on the rabbit eye. This difference in potency seemed largely due to the more effective corneal penetration of dibutoline, for only slightly less dibutoline than homatropine was required to produce a comparable degree of mydriasis when the two drugs were injected into the posterior corneal layers or into the anterior chamber.

In the human eye, 5 per cent solutions of dibutoline sulfate and of homatropine hydrobromide usually produce equivalent degrees of mydriasis, but the minimal dose of homatropine producing mydriasis is less than that of dibutoline. The latter, however, is the more effective cycloplegic. Moreover, mydriasis and cycloplegia produced by the new drug develop and wear off simultaneously; consequently, the size of the pupil and its reactivity provide convenient and reliable indications of the degree of cycloplegia produced by dibutoline. In contrast, the effects on the iris of the atropine series of drugs are much more intense than the effects on the ciliary muscles. In some young adults it is possible to induce almost complete mydriasis with neg-

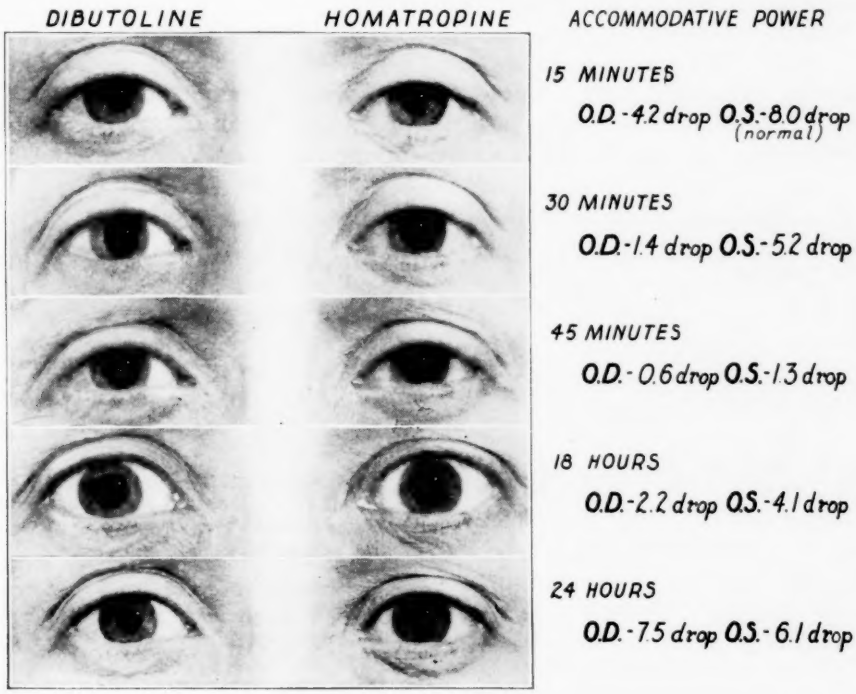


Fig. 2.—Onset and duration of mydriasis and cycloplegia in an emmetropic adult following single instillations 0.075 cc.) of a 5 per cent solution of dibutoline sulfate in the right eye and of a 5 per cent solution of homatropine hydrobromide in the left eye.

ligible loss of accommodation by means of frequent small doses of homatropine.

Twenty-four young adults had refractions under cycloplegia induced both with dibutoline and with homatropine to determine the relative effectiveness of the two drugs as cycloplegics. At the first examination the right eye received a 5 per cent solution of dibutoline sulfate and the left eye an equivalent dose of homatropine hydrobromide. A week later the process was reversed. Minimal residual accommodation was determined by adding a + 3.00 D. sphere to the cycloplegic correction for distance and determining the nearest point at which the patient could read standard 0.5 print in constant artificial illumination. Minimal residual accommodations ranging from 0.4 to 1.3 D. were found with both drugs even when careful single instillations of 0.075 cc. were made, but the average residual accommodation with dibutoline sulfate was 0.62 D., as compared with 1.08 D. with homatropine hydrobromide. The 48 eyes required an average of 0.03 D. more plus sphere with the new drug than with homatropine. The difference in the astigmatic correction was insignificant.

The onset and duration of action of dibutoline were compared with the corresponding effects of homatropine on the eyes of more than 100 patients. One drop of a 5 per cent aqueous solution of dibutoline sulfate instilled into the conjunctival sac usually produced mydriasis and cycloplegia beginning in twelve to twenty minutes and becoming maximal in forty to fifty-five minutes. The onset of its effect usually preceded that of the effects of an equal dose of homatropine by ten to fifteen minutes (fig. 2). The effects of the new drug on the intraocular muscles remained maximal for approximately three to five hours and nearly maximal for an additional three to eight hours and then wore off rapidly and completely within eight to ten hours. The average emmetropic young adult receiving the new drug was able to read in sixteen to twenty hours, and the near point of accommodation returned to normal in eighteen to twenty-four hours. With two instillations at five to ten minute intervals the duration averaged several hours longer. Cycloplegia produced by homatropine hydrobromide remained maximal for a shorter period, but wore off more gradually and over a considerably longer period, than an equivalent degree of cycloplegia produced by dibutoline (fig. 3). When equal degrees of cycloplegia had been produced by the drugs, patients usually noticed little difference in the period required to regain ability to read ordinary newsprint with effort, but reported that a longer period was required for their near vision to return completely to normal after homatropine was used. Mydriasis and hypersensitivity to light produced by homatropine persisted considerably longer than the corresponding effects of doses of dibutoline producing a comparable degree of cycloplegia. The pupil and the pupillary reflexes usually did not return to normal for thirty-six to forty-eight hours after instillation of 5 per cent homatropine hydrobromide which reduced accommodative power to less than 1 25 D. The visual disability produced by atropine and scopolamine lasted three to ten times as long as that produced by dibutoline.

The new drug did not influence the intraocular tension in 25 normal adults, varying in age from 20 to 78 years; however, the drug produced

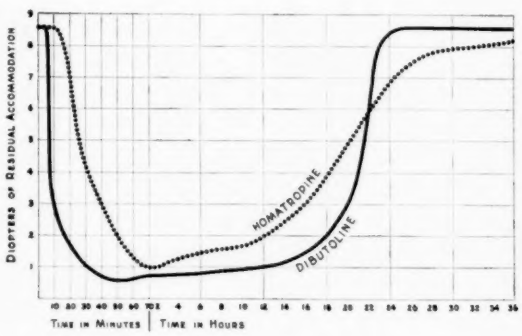


Fig. 3.—Onset and duration of comparable degrees of cycloplegia produced by 5 per cent solutions of dibutoline sulfate and of homatropine hydrobromide. The values express averages for 10 young adults.

a rise in intraocular pressure in 3 patients with suspected incipient glaucoma simplex. The average maximal rise in tension produced by single instillations of a 5 per cent solution of dibutoline sulfate was 6.3 mm. (Schiøtz), as compared with an average rise of 8.6 mm. produced in the same 6 eyes by single instillations of a 5 per cent solution of homatropine hydrobromide. The increased intraocular pressure produced by the new drug lasted an average of fourteen hours, as compared with a duration of twenty-two hours for homatropine. The series of patients is too small to permit conclusions, but the results suggest that there is less danger of a rise in intraocular pressure with the new drug than with homatropine. Possibly the vasodilation produced by homatropine contributed to the higher and more prolonged increase in tension. Congestion of the conjunctival and episcleral vessels was always more pronounced in the eyes receiv-

ing homatropine than in the eyes receiving dibutoline (fig. 4).

Most patients find that a single instillation of a fresh solution of 5 per cent homatropine hydrobromide in distilled water is more irritating than that of a 5 per cent aqueous solution of dibutoline sulfate, although buffered ($p_H$ 6.5) solutions of the homatropine salt are generally described as slightly less irritating. One or two instillations at five to ten minute intervals of a 5 per cent aqueous solution of dibutoline sulfate are well tolerated, but frequent repeated instillations create conjunctival irritation and the transitory punctate disturbances of the corneal epithelium characteristically produced by surface-active drugs.[3] These changes are perceptible only on biomicroscopic examination and do not interfere with refraction or with ophthalmoscopic examination. On the other hand, surface-active drugs not only penetrate the cornea rapidly and consistently but facilitate penetration of other drugs. Rapid and consistent absorption is particularly desirable in a drug used for cycloplegic refraction.

A 5 per cent solution of dibutoline sulfate was instilled into the conjunctival sacs of rabbits two to three times daily for periods up to four months and into those of several patients for four to six weeks. Evidences of injury to the eye other than the transitory punctate disturbance of the corneal epithelium just described were not observed by biomicroscopic or histologic methods. No evidences of hypersensitivity, idiosyncrasy or the contact type of dermatitis and conjunctivitis were noted. The series of patients and animals studied was too small to permit conclusions, but it is noteworthy that definite allergic reactions to choline esters have not been reported, while local and systemic hypersensitivity reactions to the atropine series, particularly to atropine, are not uncommon. Already dibutoline has been used satisfactorily as a substitute for drugs of the atropine series in a case of recurrent iridocyclitis in which the patient had acquired a contact type of sensitivity to the entire atropine series of drugs.

A single instillation of a 5 per cent solution of homatropine hydrobromide is most commonly used for routine cycloplegic refraction and internal examination of the eye. For purposes of comparison, a 5 per cent solution of dibutoline sulfate was used in the studies just described. It is probable that two or three instillations of a weaker concentration of the drug will prove to be more practical than a single instillation of the 5 per cent solution. It has been our experience that the 1 drop method of inducing cycloplegia is not dependable.

The use of dibutoline as a substitute for atropine or scopolamine in the treatment of infections of the anterior segment and for the relief of postoperative inflammatory conditions will be the basis of a subsequent report. Preliminary investigations indicate that for these purposes the new drug has advantages over atropine and scopolamine. Dibutoline has potent antiseptic action against the organisms which commonly cause ocular inflammation; moreover, the antibacterial action of dibutoline is synergistic with that of the mercurial antiseptics. The combined use of the two substances has proved effective in the treatment of experimental inflammatory processes of the anterior segment induced in the rabbit eye by intracorneal injections of pyogenic organisms. Also, dibutoline, like other surface-active compounds, facilitates corneal penetration of the sulfonamide compounds. The duration of maximal action of dibutoline is ideal for the treatment of inflammatory conditions of the anterior segment. Its maximal mydriatic and cycloplegic action may be maintained by two to four instillations daily; yet the effects of the drug wear off in twenty-four hours after its instillation is discontinued. In contrast, the

Fig. 4.—Comparative effects of 5 per cent solutions of dibutoline sulfate (right eye) and homatropine hydrobromide (left eye) on the conjunctival and episcleral vessels. Photograph with a blue-sensitive film.

3. Swan, K. C.: Reactivity of the Ocular Tissues to Wetting Agents, Am. J. Ophth., **27**:1118 (Oct.) 1944.

effects of atropine and scopolamine last for days and are not readily counteracted.

To provide simple mydriasis for funduscopic examination, drugs like ephedrine and eucatropine, which produce little disturbance of accommodation, are more satisfactory than dibutoline. Mydriasis produced by dibutoline is always accompanied by cycloplegia.

Some of the new drugs which we have synthesized act synergistically with atropine on the intraocular muscles.[2a] Dibutoline does not have this action, but it does facilitate corneal penetration of atropine and thereby increases the effectiveness of the latter. There is another reason that the use of dibutoline in combination with one of the atropine series may prove more desirable than administration of either drug alone; that is, patients who are relatively refractory to dibutoline seem to respond promptly to the atropine series and vice versa. Several such patients were observed.

The systemic pharmacology and toxicology of dibutoline will be reported on separately; however, it is noteworthy that the minimal lethal dose of dibutoline sulfate administered intraperitoneally in rabbits and rats is approximately 75 mg. per kilogram of body weight. The minimal lethal dose by oral administration is considerably larger, so that the danger of systemic poisoning from the instillation of dibutoline into the conjunctival sac is nil as compared with that for any drug of the atropine series. The systemic action of the new drug is characterized by an antispasmodic action on smooth muscle. Depression of the salivary secretion, effects on the central nervous system and vasomotor disturbances, such as are produced by atropine and scopolamine, do not result from dibutoline. The dose of dibutoline administered to the eye is limited by the local irritation resulting from its surface activity, rather than by the danger of systemic poisoning.

## SUMMARY AND CONCLUSIONS

The first substitutes for the atropine series of drugs effective on the eye have been synthesized by us. Dibutoline sulfate is the most useful member of the new class. In duration its effects are comparable to those produced by homatropine, but it is a more potent cycloplegic than the latter. Dibutoline does not produce paresis of the dilator fibers of the iris; therefore its mydriatic action may be enhanced by administration of epinephrine and related drugs. As a substitute for the atropine series of drugs in routine cycloplegic refraction and in internal examination of the eye, dibutoline has several advantages, notably, rapid action, a short period of visual disability and negligible systemic effects from ocular administration. Unlike the atropine series, the new drug has equal effects on the iris and the ciliary body; consequently, the size and reaction of the pupil provide a convenient indication of the degree of cycloplegia. Dibutoline has an antiseptic action, which may prove advantageous in the treatment of inflammatory conditions of the anterior segment. Its duration of action is ideal for the treatment of such processes; it also facilitates penetration of other drugs.

Dibutoline has the disadvantage that repeated instillations produce irritation of the conjunctiva and a mild, transitory, superficial punctate disturbance of the corneal epithelium. These effects are due to the surface activity of the drug.

## ABSTRACT OF DISCUSSION

Dr. S. Judd Beach, Portland, Maine: The synthesis of a new series of mydriatic and cycloplegic drugs unrelated to atropine is a major event. Dr. Swan has afforded me a short trial of dibutoline. My cases are too few to warrant my drawing any conclusions, but I wish to discuss two points in his report concerning the use of dibutoline in refraction.

Much of the recent work on cycloplegia has been unconvincing because of questionable measurement of accommodation; while none of the tests are entirely satisfactory. The authors have adhered to the classic near point test, which is probably the most effective. The value of this test lies in the response of accommodation evoked by the approach of the test object to the eye. The authors have, moreover, used test type, which appears to be better adapted to clinical examination than other symbols, such as the Duane line.

This test can be made even more exact by use of finer type than the 0.5 print, which, as the name implies, is easily read at 0.5 meter, or 20 inches, and is probably the size of type in common use for this purpose. At 20 inches the variation of 1 inch (2.5 cm.) in estimation of the near point is negligible, an error of less than ¼ D. being introduced, but if sufficient accommodation persists to permit the test type's being brought within 6 or 8 inches (15 or 17 cm.) of the eye then the variation of 1 inch introduces an error more nearly of 2 D. The 0.5 print usually corresponds to the 4 point type of printers. Use of a card showing 3 point and 2 point type is considerably more accurate.

The other point refers to the statement that the 1 drop method of inducing cycloplegia is not dependable. This statement is correct except that it implies that repeated instillations are dependable. This is a natural, but unsafe, assumption. The effect of one instillation of a solution con-

taining 2 per cent homatropine hydrobromide and paredrine hydrobromide ophthalmic 1 per cent with boric acid is cycloplegia which reaches its peak in forty-five to sixty minutes. It then recedes slowly.

In dozens of my cases it has been shown that further repeated instillations of 2 per cent homatropine hydrobromine in the regular way not only cannot be relied on to increase the cycloplegia but frequently are followed by the same slow recession, just as though no additional homatropine had been administered.

I should not be surprised if dibutoline turns out to differ from homatropine in that a second instillation regularly intensifies the cycloplegia. It is not the eyes that yield easily to cycloplegia but the eyes that resist which constitute the real test of potency of a cycloplegic drug. I have not seen many patients presenting this problem in the past few weeks. The results with the patients I have examined do not confirm the observation that dibutoline is a more potent cycloplegic than homatropine. It has usually seemed that one instillation of the solution of homatropine and paredrine hydrobromide ophthalmic is more dependable than two instillations of dibutoline sulfate; yet not much weight can be given to such a small number of observations as I have made.

There are other problems. Does instillation of 1 drop of a solution of homatropine hydrobromide and paredrine hydrobromide ophthalmic following instillation of dibutoline sulfate intensify the action more than a second instillation of dibutoline sulfate? I suspect it does. Does dibutoline intensify the cycloplegia after homatropine has been instilled? The authors suggest that the two drugs be combined.

This study seems the most ingenious and promising contribution to cycloplegia in recent years. The merits of the new cycloplegic seem to be increased safety, greater speed of action and of recovery and lack of annoyance to the patients.

Dr. Jonas S. Friedenwald, Baltimore: This development of a new group of cycloplegics is a brilliant achievement. Dr. Swan's reports seem to be extremely conservative; like him, I should wish more extensive use of the drug before its full value can be determined. All eagerly await further reports of its action, on the basis of which one can determine for what particular conditions the use of dibutoline has advantages equal, superior or inferior to those of the atropine series.

There are, however, patients who already can be said to have been greatly benefited by this drug, namely, patients who have acquired hypersensitivity to the atropine series and treatment of whose condition is hopeless without this drug. I was able to test this drug on such a patient. In spite of his being hypersensitive to scopolamine and similar drugs, he tolerated dibutoline well, and I produced mydriasis in his inflamed iris, which I had not been able to do for several weeks, owing to the contraindication to the use of atropine.

Dr. William H. Crisp, Denver: Every ophthalmologist must have felt at times that he would like to hear of a new cycloplegic which would overcome all the difficulties experienced with the old drugs. Apparently, dibutoline sulfate is not entirely free from toxic effects, and I am afraid that there are apt to be objections to any new synthetic compound.

Unfortunately, some of the experimental timing in handling a drug of this kind cannot be repeated in ordinary busy office practice. I work as nearly as possible on the appointment system, but I usually drag behind in the course of a busy day, with many interruptions. The result is that I have to fear some loss of efficiency of homatropine.

To eliminate the toxic factor in the use of a cycloplegic, I try to make sure that the drug is instilled shortly after a fairly substantial meal, so that there is food in the stomach when the drug trickles through the nose and the nasopharynx and down into the stomach. I avoid a good deal of disturbance in that way.

Apart from its toxic qualities and the rather long period required for recovery, scopolamine is a valuable cycloplegic. For refraction I use the drug only in my office, always watching carefully for the possibility of a troublesome reaction. I have been surprised at times at the precision of its action in a young person with normally active accommodation after a single instillation of a 1:500 solution of the hydrobromide. Frequently, after one instillation of the drug, with a wait of not less than an hour, the patient has promptly rejected the addition of a — ⅛ D. sphere to a plus sphere with which I seemed to have worked out the accurate correction at the trial case.

In using atropine for refraction, I do not use quite so strong a solution as some ophthalmologists. With children I try to have it used six times immediately after mealtime for two days prior to my examination in a strength of 1:240, i. e. 1 grain (0.065 Gm.) in 4 fluidrachms, or ½ grain (0.032 Gm.) in 2 fluidrachms. I carefully advise the parents not so much against occlusion of the lacrimal passages as that they instil only a single drop, having already measured how much they must draw up into the dropper to get a single drop, and that they always make the instillation after a fairly substantial meal. I seldom have any troublesome toxic reactions in young children.

Dr. Kenneth C. Swan, Iowa City: I sincerely appreciate the comments of the discussers,

and I hope that the drug will live up to their expectations.

Dr. Beach is justified in his criticism of our use of 0.5 print. We selected this size print not because it provided a more accurate test but because it has been used in many previous studies with other cycloplegics. We wished the members of the medical profession to be able to compare our work with that of previous investigators. After hearing Dr. Beach, I realize that we erred in not selecting a more accurate test.

Dibutoline and the atropine series do not have a true synergistic action on the intraocular muscles; however, there is an apparent synergism because the new drug, being surface active, facilitates corneal penetration of atropine and thereby increases the concentration of the latter in the eye.

Use of the new drug in combination with drugs of the atropine series might be more satisfactory in a crowded office. As Dr. Crisp mentioned, a refractionist gets behind in his work when satisfactory cycloplegia is not obtained in a patient. We have observed several patients who are refractory to homatropine but not to dibutoline and vice versa. The combination of the two drugs would eliminate many of the delays due to refractory patients.

University Hospital.

# ESTIMATION OF UNCORRECTED VISUAL ACUITY IN MALINGERERS

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MEDICAL CORPS, ARMY OF THE UNITED STATES

Uncorrected visual acuity [1] is an important basis for physical classification in the Army. Consequently, some soldiers, in order to escape combat service, simulate decreased visual acuity. In civilian life, in compensation or accident cases, persons also often conceal their true visual status. It is absurd in examination of such patients to rely solely on a subject's statements as to his visual acuity. By following the routine about to be described, one may in most cases estimate with reasonable accuracy the uncorrected visual acuity of ametropic persons.

A careful retinoscopic study should be made after complete cycloplegia has been obtained. Slit lamp and ophthalmoscopic examinations should rule out opacities in the media and lesions in the fundi. Neurologic conditions that cause central scotoma are not detectable with the ophthalmoscope. The history, the circumstances surrounding the case, the perimetric and tangent screen plottings at varying distances usually all aid in establishing a diagnosis of retrobulbar neuritis, toxic amblyopia or interference with the visual pathways. In the case of a soldier, the visual requirements of the occupation that was followed before induction should be considered. Further, it is unlikely that a person of fair intelligence who rather suddenly became amblyopic would have failed to seek immediate medical aid and have waited until induction into the Army or overseas service became imminent before establishing the existence of the visual defect.

The malingerer is apt to do unphysiologic things. He frequently affects photophobia, usually of an intense form. He is likely to narrow the palpebral fissures and blink rapidly. Sometimes he affects difficulty in walking about in dim illumination, despite the fact that perimetric examination may have revealed normal peripheral fields. Invariably, he overplays his part. He simulates a decreased visual acuity which is far below a reasonable correlation with the refractive error.

Occasionally it is possible to trick a simulator of poor visual acuity into conceding somewhat better vision than he had intended to admit by allowing him to see only test charts which start with smaller letters than the conventional size for the 200 feet (60 meter) distance. Repeated examinations in different rooms at different distances and with different charts and projectors also may confuse the malingerer.

The best possible correction for the refractive error should be estimated from the retinoscopic examination and from the power of the correction that is being worn. It must be remembered that some malingerers will deliberately wear lenses that are too strong. Subjective aid usually can be obtained from the examinee. Most simulators, while under the effects of a cycloplegic, can be coaxed, argued or ordered into stating whether, for the size of letter that they admit seeing, a lens is better or worse, whether it makes the letters appear straighter or more tilted, smaller or larger, and so on. In this way a fairly accurate approximation of the true correction can be obtained. A lens combination that is approximately correct for test letters which subtend a large visual angle is also approximately correct for letters at the true minimum visual angle. In young persons (under 30)

1. Visual acuity may be said to vary inversely with the minimum visual angle. This is the angle subtended at the nodal point of the eye by the smallest resolvable image. Snellen introduced the concept that a 1 minute angle represents normal visual acuity, and he designed his test types according to the plan of having the component parts of the Roman capital letters, the lines, the spaces between the lines and the breaks all of such width as to subtend 1 minute angles at certain designated distances, while the letters as a whole are enclosed in squares the sides of which subtend 5 minute angles at the same distances.

The tangent of an angle of 1 minute is 0.00029. Therefore the width of the lines, spaces and breaks of the letters on the 20 foot (6 meter) line should equal $20 \times 0.00029$, or 0.0058 foot ($6 \times 0.00029$, or 0.00174 meter). At greater distances the widths must increase by the same ratio as that between the greater distance and 20 feet. Thus, at 100 feet (30 meters) a 1 minute angle is subtended by $100/20 \times 0.0058$ foot, or by a width of 0.029 foot ($30/6 \times 0.00174$ meter, or by a width of 0.0087 meter).

Disease of the eye, disease of the visual nerve paths and errors of refraction all decrease visual acuity and increase the minimum visual angle. Up to about 5 degrees, in natural trigonometric functions, the value of the tangent increases directly and in the same ratio as the angle. Thus, if at 20 feet a person cannot see more than the 40 foot (12 meter) letters, his minimum visual angle is 2 minutes.

TABLE 1.—*Correlations of Visual Acuity and Required Correction* *

| Uncorrected Visual Acuity on Snellen Chart | Required Dioptric Powers of Correcting Lenses Necessary for 20/20 Vision | | | | |
|---|---|---|---|---|---|
| | Minus Spheres (Myopia) | Minus Cylinders (Simple Myopic Astigmatism) | Minus Spheres Combined with Minus Cylinders (Compound Myopic Astigmatism) | Minus Spheres Combined with Plus Cylinders (Mixed Astigmatism) | Plus Cylinders (Hypermetropic Astigmatism) |
| 20/20 | −0.12 D. sph. | −0.25 D. cyl., ax a | | | +0.50 D. cyl., ax a |
| 20/25 | −0.25 D. sph. | −0.50 D. cyl., ax a | −0.12 D. sph. ⊂ −0.25 D. cyl., ax a | −0.25 D. sph. ⊂ +0.50 to +0.75 D. cyl., ax a | +0.75 D. cyl., ax a |
| 20/30 | −0.37 to −0.50 D. sph. | −0.75 D. cyl., ax a | −0.25 D. sph. ⊂ −0.50 D. cyl., ax a<br>−0.50 D. sph. ⊂ −0.25 D. cyl., ax a | −0.75 to −1.00 D. sph. ⊂ +1.00 to +1.25 D. cyl. | +1.00 D. cyl., ax a |
| 20/40 | −0.62 to −0.75 D. sph. | −1.00 D. cyl., ax o<br>−1.25 to −1.50 D. cyl., ax v or h | −0.25 D. sph. ⊂ −0.75 D. cyl., ax o, or −1.00 D. cyl., ax v or h<br>−0.50 D. sph. ⊂ −0.50 D. cyl., ax o, or −0.75 D. cyl., ax v or h | −0.50 to −1.25 D. sph. ⊂ +1.25 to +2.00 D. cyl. | +1.25 to +1.50 D. cyl., ax o<br>+1.25 to +1.75 D cyl., ax v<br>+1.25 to +2.00 D. cyl., ax h |
| 20/50 | −1.00 D. sph. | −1.25 to −1.50 D. cyl., ax o<br>−1.75 to −2.25 D. cyl., ax v<br>−1.75 to −2.50 D. cyl., ax h | −0.25 D. sph. ⊂ −1.00 to −1.25 D. cyl., ax o, or −1.25 to −1.75 D. cyl., ax v or h<br>−0.50 D. sph. ⊂ −0.75 to −1.00 D. cyl., ax o, or −1.00 to −1.25 D. cyl., ax v or h<br>−0.75 D. sph. ⊂ −0.25 to −0.50 D. cyl., ax a | −0.50 to −1.75 D. sph. ⊂ +2.25 to +2.75 D. cyl. | +1.50 to +2.00 D. cyl., ax o<br>+1.75 to +2.25 D. cyl., ax v<br>+2.00 to +2.50 D. cyl., ax h |
| 20/70 | −1.25 to −1.50 D. sph. | −1.75 to −2.25 D. cyl., ax o<br>−2.25 to −2.50 D. cyl., ax v<br>−2.25 to −2.75 D. cyl., ax h | −0.50 D. sph. ⊂ −1.00 to −1.25 D. cyl., ax o, or −1.25 to −1.50 D. cyl., ax v or h<br>−0.75 D. sph. ⊂ −0.50 to −0.75 D. cyl., ax o, or −0.75 to −1.00 D. cyl., ax v or h<br>−1.00 D. sph. ⊂ −0.50 D. cyl., ax o, or −0.75 D. cyl., ax v or h | −0.50 to −2.50 D. sph. ⊂ +2.75 to +3.25 D. cyl. | +2.25 to +2.50 D. cyl., ax o<br>+2.50 to +2.75 D. cyl., ax v<br>+2.50 to +3.00 D. cyl., ax h |
| 20/100 | −1.50 to −1.75 D. sph. | −2.50 to −3.00 D. cyl., ax o<br>−2.75 to −3.25 D. cyl., ax v<br>−3.00 to −3.50 D. cyl., ax h | −0.50 D. sph. ⊂ −1.50 to −2.00 D. cyl., ax o, or −1.75 to −2.25 D. cyl., ax v, or −1.75 to −2.00 D. cyl., ax h<br>−0.75 D. sph. ⊂ −1.00 to −1.50 D. cyl., ax o, or −1.25 to −1.75 D. cyl., ax v, or −1.50 to −2.00 D. cyl., ax h<br>−1.00 D. sph. ⊂ −0.75 to −1.00 D. cyl., ax o, or −1.00 to −1.25 D. cyl., ax v, or −1.00 to −1.50 D. cyl., ax h<br>−1.25 D. sph. ⊂ −0.50 D. cyl., ax o, or −0.75 to −1.25 D. cyl., ax v or h<br>−1.50 D. sph. ⊂ −0.25 to −0.50 D. cyl., ax a | −0.50 to −3.00 D. sph. ⊂ +3.25 to +3.50 D. cyl. | +2.50 to +2.75 D. cyl., ax o<br>+2.75 to +3.25 D. cyl., ax v<br>+3.00 to +3.50 D. cyl., ax h |
| 20/150 | −2.00 to −2.25 D. sph. | −3.00 to −3.25 D. cyl., ax o<br>−3.25 to −3.75 D. cyl., ax v<br>−3.50 to −4.00 D. cyl., ax h | −0.50 D. sph. ⊂ −2.25 to −2.50 D. cyl., ax o, or −2.50 to −3.00 D. cyl., ax v, or −2.75 to −3.25 D. cyl., ax h<br>−0.75 D. sph. ⊂ −1.75 to −2.25 D. cyl., ax o, or −2.00 to −2.50 D. cyl., ax v, or −2.25 to −2.75 D. cyl., ax h<br>−1.00 D. sph. ⊂ −1.25 to −1.75 D. cyl., ax o, or −150 to −2.00 D. cyl., ax v, or −1.75 to −2.25 D. cyl., ax h<br>−1.25 D. sph. ⊂ −0.75 to −1.25 D. cyl., ax o, or −1.25 to −1.50 D. cyl., ax v, or −1.50 to −2.00 D. cyl., ax h<br>−1.50 D. sph. ⊂ −0.75 D. cyl., ax o, or −1.00 D. cyl., ax v, or −1.00 to −1.25 D. cyl., ax h<br>−1.75 D. sph. ⊂ 0.50 D. cyl., ax o, or −0.50 to −0.75 D. cyl., ax v or h<br>−2.00 D. sph. ⊂ −0.25 to −0.50 D. cyl., ax a | −0.50 to −3.50 D. sph. ⊂ +3.75 to +4.00 D. cyl. | +2.75 to +3.00 D. cyl., ax o<br>+3.25 to +3.75 D. cyl., ax v<br>+3.75 to +4.00 D. cyl., ax h |

| | | | | | |
|---|---|---|---|---|---|
| 20/200 | −2.50 to −2.75 D. sph. | −3.50 to −3.75 D. cyl., ax o<br>−4.00 to −4.50 D. cyl., ax v<br>−4.00 to −4.50 D. cyl., ax h | −0.50 D. sph. ⊂ −2.75 to −3.00 D. cyl., ax o, or<br>−3.00 to −3.50 D. cyl., ax v, or<br>−3.25 to −3.75 D. cyl., ax h<br>−1.00 D. sph. ⊂ −1.75 to −2.25 D. cyl., ax o, or<br>−2.00 to −2.50 D. cyl., ax v, or<br>−2.50 to −3.00 D. cyl., ax h<br>−1.50 D. sph. ⊂ −1.00 to −1.50 D. cyl., ax o, or<br>−1.25 to −1.75 D. cyl., ax v, or<br>−1.75 to −2.00 D. cyl., ax h<br>−2.00 D. sph. ⊂ −0.50 to −0.75 D. cyl., ax o, or<br>−0.75 to −1.25 D. cyl., ax v or h<br>−2.25 D. sph. ⊂ −0.50 to −0.75 D. cyl., ax a | −0.75 to −3.75 D. sph. ⊂ +4.00 to +4.50 D. cyl. | +3.25 to +3.75 D. cyl., ax o<br>+3.75 to +4.50 D. cyl., ax v<br>+4.25 to +4.75 D. cyl., ax h |
| 20/250 | −3.00 to −3.25 D. sph. | −4.00 to −4.50 D. cyl., ax o<br>−4.50 to −5.00 D. cyl., ax v<br>−4.75 to −5.75 D. cyl., ax h | −0.75 D. sph. ⊂ −3.00 to −3.25 D. cyl., ax o, or<br>−3.25 to −3.75 D. cyl., ax v, or<br>−3.50 to −4.00 D. cyl., ax h<br>−1.25 D. sph. ⊂ −2.25 to −2.75 D. cyl., ax o, or<br>−2.50 to −3.00 D. cyl., ax v, or<br>−2.75 to −3.25 D. cyl., ax h<br>−1.75 D. sph. ⊂ −1.75 to −2.25 D. cyl., ax o, or<br>−2.25 to −2.75 D. cyl., ax v or h<br>−2.25 D. sph. ⊂ −1.00 to −1.50 D. cyl., ax o, or<br>−1.50 to −1.75 D. cyl., ax v or h<br>−2.75 D. sph. ⊂ −0.50 to −0.75 D. cyl., ax o, or<br>−0.75 to −1.25 D. cyl., ax v or h | −0.75 to −4.50 D. sph. ⊂ +4.50 to +5.25 D. cyl. | +4.00 to +4.75 D. cyl., ax o<br>+4.75 to +5.25 D. cyl., ax v<br>+5.00 to +5.75 D cyl., ax h |
| 20/300 | −3.25 to −3.75 D. sph. | −4.75 to −5.25 D. cyl., ax o<br>−5.25 to −5.75 D. cyl., ax v<br>−6.00 to −6.25 D. cyl., ax h | −1.00 D. sph. ⊂ −3.50 to −4.00 D. cyl., ax o, or<br>−3.75 to −4.50 D. cyl., ax v, or<br>−4.25 to −4.75 D. cyl., ax h<br>−1.75 D. sph. ⊂ −2.50 to −3.00 D. cyl., ax o, or<br>−2.75 to −3.25 D. cyl., ax v, or<br>−3.00 to −3.50 D. cyl., ax h<br>−2.50 D. sph. ⊂ −1.25 to −1.50 D. cyl., ax o, or<br>−1.50 to −2.00 D. cyl., ax v, or<br>−1.75 to −2.25 D. cyl., ax h<br>−3.00 D. sph. ⊂ −0.50 to −0.75 D. cyl., ax o, or<br>−0.75 to −1.25 D. cyl., ax v or h | −0.75 to −5.00 D. sph. ⊂ +5.25 to +6.00 D. cyl. | +4.75 to +5.25 D. cyl., ax o<br>+5.25 to +5.75 D. cyl., ax v<br>+5.75 to +6.00 D. cyl., ax h |



Beyond visual acuities of 20/300 there were not available sufficient cases in which high cylindric errors occurred to permit statistical correlation. The infrequent cases that were encountered conformed approximately to the general pattern of the relation between visual acuity and correcting lens power. A few examples follow

| Uncorrected Visual Acuity on Snellen Chart | Minus Spheres (Myopia) | Actual Visual Acuity | Required Correction | Visual Acuity Usually Associated with the Spherical Component | Visual Acuity Usually Associated with the Cylindric Component | Combined, or Additive, Effect (Compare with Actual Acuity) |
|---|---|---|---|---|---|---|
| 20/350 | −4.00 to −4.25 D. sph. | 20/400 | −4.00 D. sph. ⊂ −1.75 D cyl., ax 3 | 20/350 | 20/50 | 20/(350 + 50) |
| 20/400 | −4.50 to −4.75 D. sph. | 20/450 | −3.00 D. sph. ⊂ −3.50 D. cyl., ax 68 | 20/250 | 20/200 | 20/(250 + 200) |
| 20/450 | −5.00 to −5.25 D. sph. | 20/500 | −3.00 D. sph. ⊂ −6.00 D. cyl., ax 176 | 20/250 | 20/300 | 20/(250 + 300) |
| 20/500 | −5.50 to −6.00 D. sph. | 20/500 | −4.75 D. sph. ⊂ −1.25 D. cyl., ax 124 | 20/400 | 20/50 | 20/(400 + 50) |
| 20/600 | −6.25 to −6.75 D. sph. | 20/600 | −5.75 D. sph. ⊂ −2.75 D. cyl., ax 30 | 20/500 | 20/100 | 20/(500 + 100) |

* In this table, and in table 2, a indicates any axis; o, the oblique axis (from 10 to 80 degrees and from 100 to 170 degrees); v, the vertical axis (from 80 to 100 degrees), and h, the horizontal axis (from 180 to 10 degrees and from 170 to 180 degrees)

with hypermetropia the paralysis of accommodation need not be considered if the amount of hypermetropia is less than 4.5 D. Under these conditions the hypermetropia itself does not decrease visual acuity. Concomitant astigmatism decreases visual acuity in the same manner as it would in the absence of any hypermetropia.

After correcting lenses have been placed before the eyes, the cover test should be used to determine the presence or absence of strabismus. Care must be taken that the examinee actually fixates the light. The cover test is worthless if the subject does not consciously follow the light all the time. Observation of the position of the image of the light on the cornea will determine this. An amblyopic eye may fixate eccentrically, and this fact will indicate that a central scotoma is present.

Strabismus is not present in all eyes with unilateral amblyopia. Therefore it is necessary to find out whether the presumably amblyopic eye is fixating the test letters. The examiner can do this by suddenly interposing a horizontal prism of 5 or 6 D. before the doubtful eye while the subject, with both eyes open, is slowly reading some test types. Fusional movements of both eyes will occur if the eye behind the prism is fixating. In my experience such fixation, while the other eye has corrected vision of 20/20, indicates a correctable visual acuity of 20/40 or better. An eye with less visual acuity than this does not fixate during binocular vision if the other eye is good and therefore will not make a fusional movement under such circumstances.

It is well for the examiner to keep in mind two little known types of amblyopia. The first might be called "amblyopia of anisometropia." It is unilateral and is not accompanied by strabismus (if strabismus were present it would of course be amblyopia ex anopsia). When the refractive error of one eye is greater than that of the other by more than 2.5 D., it not infrequently happens that the more ametropic eye is found to be amblyopic.

The second type might be called "amblyopia of uncorrected ametropia." Usually it is bilateral. Uncorrected refractive errors may be accompanied by decreased visual acuity which is not immediately correctable by the wearing of proper lenses. After some time, usually several months, the visual acuity gradually will improve.

## VISUAL ACUITY CORRELATIONS

If it has been established that an eye is free from visible disease and that it fixates, the uncorrected visual acuity can be estimated accurately if the approximate refractive error is known. The accompanying tables represent correlations and deductions that have been made on the basis of over 6,000 refractions done on persons who had no reasons for withholding the truth. They were young adults of both sexes, under 30, who presented no encroachment of the upper eyelids on the pupillary area of the cornea and whose best corrected vision was 20/20 or better.

The resolving power of the eye varies somewhat from person to person. It is dependent on many factors, such as the size of the pupil, the location and curvature of the refracting elements with respect to each other, the structure of the macula and, possibly also, the structure and functional capabilities of the occipital cortex. Nevertheless, whenever a dishonest subject makes it necessary for an ophthalmic examiner to estimate the true visual acuity, the accompanying correlations will serve as a fair basis for appraisal.

It must be kept in mind that the correlations are expressed in terms of visual acuity measured by the Snellen test types (Roman capital letters). These test types are not as accurate as broken circles but are much more practicable. It is easier to guess a distorted letter than the position of the break in a blurred circle. Consequently, the visual acuity will appear slightly better with a Snellen test chart than with a chart of broken circles.

Consideration of the table of correlations reveals a number of points which deserve comment.

Eyes with astigmatism of identical amounts show small, but definite, variations in uncorrected visual acuity depending on the position of the axis of astigmatism. Astigmatism that requires the correcting cylinder in the horizontal axis (from 180 to 10 degrees and from 170 to 180 degrees) is associated with a slightly greater visual acuity than the astigmatism of equal amount which requires a correcting cylinder in the vertical axis (from 80 to 100 degrees). The latter form, in turn, is associated with a slightly greater visual acuity than the astigmatism requiring a cylinder in the oblique axis (from 10 to 80 degrees and from 100 to 170 degrees). Very likely the structure of the Snellen letters accounts for this, and with broken circles this variation probably could not be shown.

Simple myopic and simple hypermetropic astigmatism of the same amount are associated with practically identical decreases of visual acuity. Offhand, one would think that hypermetropic astigmatism should be associated with better visual acuity than myopic astigmatism. Theoretically, the hypermetrope can focus alter-

nately on the two planes of ametropia. Yet this does not seem to be the case.

A certain correspondence exists between cylindric and spherical corrections for myopia. Simple myopic astigmatism requiring a diverging cylinder in the horizontal axis is accompanied by about the same uncorrected visual acuity as simple myopia requiring a sphere of from 45 to 55 per cent of the numerical value of the cylinder. For example: The visual acuity that corresponds to an ametropia requiring a —2.50 D. cylindric correction in the horizontal axis is 20/70. The same visual acuity usually corresponds to a myopia of — 1.12 D. ($0.45 \times 2.50 = 1.125$). Likewise, a minus cylinder in the vertical axis can be correlated with a minus sphere of about 50 to 60 per cent of the same numerical dioptric power, while in the oblique axis the correspondence is about 60 to 70 per cent.

TABLE 2.—*Simplified Table Showing Approximate Relation of Visual Acuity and Required Correction* *

| Uncorrected Visual Acuity on Snellen Test Chart | Power of Correcting Sphere for Myopia or Absolute Hypermetropia (D.) | Required Cylindric Correction for Simple Myopic and Hypermetropic Astigmatism (D.)† | | |
|---|---|---|---|---|
| | | Oblique Axis | | Horizontal Axis |
| 20/30 | 0.50 | 0.75 | to | 1.00 |
| 20/40 | 0.75 | 1.00 | to | 1.50 |
| 20/50 | 1.00 | 1.50 | to | 2.00 |
| 20/70 | 1.25 | 1.75 | to | 2.50 |
| 20/100 | 1.50 | 2.25 | to | 3.00 |
| 20/150 | 2.00 | 2.75 | to | 4.00 |
| 20/200 | 2.50 | 3.50 | to | 4.50 |
| 20/250 | 3.00 | 4.25 | to | 5.50 |
| 20/300 | 3.50 | 5.00 | to | 6.25 |
| 20/350 | 4.00 | | | |
| 20/400 | 4.50 | | | |
| 20/450 | 5.00 | | | |
| 20/500 | 5.50 | | | |
| 20/600 | 6.50 | | | |

* Spherical lens power may be converted into equivalent cylindric lens power, corrective for identical amounts of decreased visual acuity, by multiplying the dioptric value of the sphere by 1.4 for cylinders in the oblique axis, by 1.6 for cylinders in the vertical axis and by 2 for cylinders in the horizonal axis. For visual acuities lower than 20/150, the multiplication factor is 1.8 for cylinders in the horizontal axis.

Conversely, the corresponding spherical lens which corrects the same visual acuity as a specific cylindric lens can be obtained by multiplying the dioptic power of the cylinder by 0.50 when the axis of the cylinder is horizontal (by 0.55 when the visual acuity is less than 20/150), by 0.60 when the axis of the correcting cylinder is vertical and by 0.70 when the axis is oblique.

† Values for the vertical axis are intermediate.

In a case of mixed astigmatism the retina lies somewhere between the two principal focal planes, and the condition may be regarded as being composed of two components—a myopic astigmatic component and a hypermetropic astigmatic component at the opposite axis. Thus, in the prescription — x sph. ⊃ + y cyl. z axis, which is the correction for mixed astigmatism, — x represents the strength of the diverging cylinder, at right angles to axis z, that is required to bring the first focal line back on the retina, and y – x represents the power of the converging cylinder at z axis that will bring the second focal line forward to the retina.

Decreased visual acuity is synonymous with an increase in the minimum visual angle. If an ametropic condition, such as mixed astigmatism, represents the cumulative effect of two component conditions, the increased minimum angle resulting from the combination should equal the sum of the two minimum visual angles corresponding to the component ametropic factors. Thus, if 20/a expresses the decreased visual acuity resulting from one of the astigmatic components, and 20/b, the acuity resulting from the second component (both a and b must, of necessity, be greater than 20), then the resultant combined decreased visual acuity will equal 20/ (a + b). It is permissible to compute in this manner because, as already stated in footnote 1, for the tiny angles used in measuring visual acuity, the value of the tangent increases directly, and in the same ratio, as the size of the angle. The fractional notation used in expressing visual acuity really is a representation of the ratio of the tangent of the standard 1 minute angle to the tangent of the minimum visual angle.

In order to estimate the visual acuity in cases of uncorrected mixed astigmatism, one simply separates the estimated or known correction into its two cylindric components. Then, from the table of correlations the visual acuity corresponding to each component can be obtained. These two values must be combined, as just indicated. For example: The required correction is — 1.75 D. sph. ⊃ + 3.00 D. cyl., axis 90. This is identical with a — 1.75 D. cyl., axis 180 combined with a + 1.25 D. cyl., axis 90. The visual acuity which corresponds to the first component is 20/50, and that which corresponds to the second component is 20/40. Combined, these two values equal 20/90, which is practically 20/100, and a reasonable estimate.

A similar method can be used for computing the approximate visual acuity in cases of compound myopic astigmatism. The spherical and the cylindric component may be estimated separately and then combined.

Hypermetropia has been mentioned already. Facultative hypermetropia, by itself, does not involve any decrease in uncorrected visual acuity. Absolute hypermetropia affects the minimum visual angle in about the same way as does myopia. For example, if there is 2 D. of hypermetropia that cannot be overcome by the accommodation, the visual acuity probably is 20/150; for 1.5 D. the acuity probably is 20/70.

# QUEREAU-PUTNAM TROPOPHOROMETER

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The instrument here described has been designed to measure deviations of the eyes in cases of squint and heterophoria. It will measure vertical deviations in the six cardinal directions, as well as horizontal deviations for distance and near vision. Its accuracy, especially in objective tests, is greater than that of any other method of which we know.

The principle employed is the movement of two light sources to describe two spheres the centers of which are substantially coincident with the centers of rotation of the eyeballs (fig. 1). The two light sources are independently movable and are shielded in such a manner that a narrow beam is visible only to the eye about the center of which it travels. The light is visible to the observer as a reflex on the cornea of the eye fixing it. Each light is mounted on a movable arm which permits it to be swung beyond the limit of rotation of the eye in any direction. The visual line from a light to its corresponding eye can be considered a radius of the sphere; hence any movement of the light in any direction about the eye does not alter the distance of fixation.

The angle above or below the zero position is registered on scales at either side of the patient's head. Lateral deviations from the position of eyes front, or the zero position, are indicated on a scale at the base of the instrument. Lateral rotations of each eye are registered on the same scale. A differential scale is attached to one of the scale pointers, so that the angular difference between the visual lines may be read directly. Scales may be calibrated in arc degrees or in prism diopters.

In order that the centers of the spheres described by the lights shall coincide with the centers of rotation of the corresponding eyes, all scales are set at zero, and the adjusting screws at either side of the base are turned until the distance between the lights is the same as the interpupillary distance. Next, the chin and head rest is adjusted to move the head up or down, or backward or forward, until an imaginary line between the arm pivots at either side of the patient's head passes approximately through the centers of rotation of the eyes.

On the base of the instrument, in front of the differential scale, are two rheostats for control of the brightness of the fixation lights. In front of these are switches and a flashing button. By means of these devices, both lights may be lighted continuously, either light may be left on while the other is flashed by pressing the flashing button or both lights may be flashed on and off alternately.

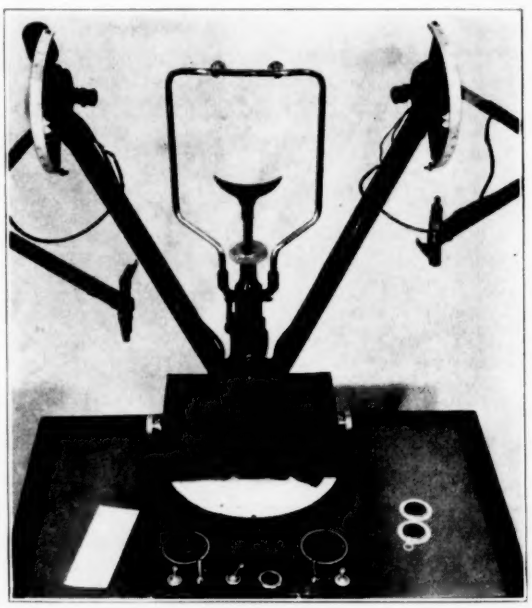

Fig. 1.—Tropophorometer, showing scales and shielded lights which throw a narrow beam into the eye from the ends of the supporting arms.

Both the arms supporting the lights may be shortened or lengthened. This adjustment moves the light either directly toward or directly away from the center of the eye, changing only the radius of the sphere or the distance of fixation, but not disturbing any directional relationships. Because of this provision and the fact that each light moves on a separate sphere, there is no

Demonstrated April 19, 1944, at meeting of the Reading Eye, Ear, Nose and Throat Society.

position in which one light will interfere with the other or will be shielded from view by it. The two lights may appear superimposed to the patient at any point in the field of binocular fixation.

With the lights placed 15 inches (38 cm.) in front of the patient's eyes, an angular separation of 1 arc degree is equivalent to a linear separation of 7.5 mm. Most patients can detect a separation of less than 1 mm.; hence a deviation of 1.75 mm., which represents 0.25 arc degree, or 0.5 prism diopter, is easily recognized. This accuracy of measurement is present in the entire field of fixation.

### METHOD OF MEASUREMENT AT FIFTEEN INCHES

The instrument may be used in subjective determinations with the screen parallax test or the Maddox rod or red glass or simply by the examiner's asking the patient to announce when the two lights are superimposed. If larger targets are desired, polarized or chromatic shielding may be used. With polarized shielding a polarizing medium is placed in front of each target and a polarizing filter in front of each eye. The light from the two targets is polarized in planes at right angles to each other. Each filter is polarized in the same plane as the corresponding target. With chromatic shielding the targets are of complementary colors, such as red and green. A filter of the same color as the corresponding target is placed in front of each eye. With each type of shielding the right eye can see only the right target and the left eye only the left target. Objectively, the instrument may be employed with the cover test in a lighted room, and here lies its greatest field of usefulness.

The screen parallax test may best be made in a darkened room. With the two lights on and placed near each other in any part of the field of fixation, a cover is passed from one eye to the other and the position of the lights changed until the patient sees no apparent movement, just as the apparent motion of a single test object is neutralized with prisms. Instead of the use of a cover, each light may be flashed alternately.

The light directed toward the left eye is termed the left light, and the light directed toward the right eye, the right light. No matter how closely the lights are brought together, the patient can see only the left light with his left eye and only the right light with the right eye. This continues to be true no matter to what degrees the visual lines cross. With the two lights set at the same level, a patient with left hyperphoria of 2 degrees will see, on alternate flashing of the lights, what appears to be a single light which moves up and down. When the examiner moves the left eye up 2 degrees, the apparent motion will cease. The amount of deviation may be read from the vertical scales.

The Maddox rod may be used as follows: In measurement of a lateral deviation, for example, the red Maddox rod may be held in front of the left eye in a vertical position. The rays from the left light will be seen by the left eye as a vertical red line. The right eye sees only its corresponding white light, which is not visible to the left eye. The patient will now say that the red line is to the right or to the left of the light. It is necessary to move only one of the lights until the red line passes through the light. The red line may now be flashed off and on a few times to eliminate the error caused by fusion, the patient being asked to give the position of the red line when he first sees it. The amount of the deviation is read from the horizontal scale.

Fig. 2.—Measurement of vertical deviation by the cover test with the eyes turned up 30 degrees and to the left 30 degrees. The lights have been separated 16 prism diopters laterally, the amount of the patient's exotropia for a distance of 15 inches (38 cm.). The right eye can see only the right light. When the cover was shifted to the right eye, the left eye moved down to fix the left light. The left light was raised until this downward motion was neutralized, and the amount of the left hypertropia was read from the scale.

A dark red glass held over one eye may be employed. The patient will then see one white and one red light, each light being visible only to its corresponding eye. The examiner then moves one of the lights vertically and horizontally

until the patient sees the red light superimposed on the white light. Actually, the lights will be separated by the amount of the vertical and lateral deviation.

Objectively, the instrument may be used in conjunction with the cover test (figs. 2 and 3). The cover is passed from side to side, and the movement of the eye under cover is watched as the cover is passed to the other eye. If the eye moves in to fix its corresponding light, this light is moved out until all lateral motion is neutralized. It may now be found that the covered eye moves up or down to fix its light when the cover is removed. The lights are

Fig. 3.—The lights have been moved to a point 30 degrees down and 30 degrees to the left of the position of eyes front. When the cover was moved from the right to the left eye, the right eye moved up to fix. The right light was moved down until this motion was neutralized. Left hypertropia was greatest in this field, an observation which indicated paresis of the left inferior rectus muscle.

moved vertically until this motion is neutralized, and the amount of the horizontal and vertical deviation is read from the scales. This test may be carried out in all the cardinal directions as easily as in the position of eyes front. A clear view of the eyes is afforded the examiner at all times. The corneal reflex from each light may easily be seen in a lighted room. This permits the examiner to be sure the patient is fixing properly. In addition, the angle of squint, both horizontal and vertical, may be approximately measured by centering the corneal reflexes on the eye. This is helpful in the case of young children and reduces the amount of subsequent screening. Finally, the deviation of a blind eye in any direction may be measured in this way. Of course an approximate allowance for the angle alpha should be made.

### METHOD OF MEASUREMENT OF DEVIATION AT TWENTY FEET

The lateral or vertical deviation for distance may be measured accurately both by the subjective and by the objective method. A 20/40 letter, cut from a vision chart, is placed at least 20 feet (6 meters) away, having been fastened to a wall with adhesive tape. The advantage of a test letter is that the patient must focus his eye for that distance in order to read it.

With the subjective method, the patient's left eye, for example, is covered, and he is asked to direct his right eye to the distant test letter. The right light is now brought to a position at which the patient sees it directly below the test letter. The light is now just below the visual line of the right eye as it fixes the distant object, and, without its lateral position's being disturbed, the light is pushed up out of view. In this way there is no distraction to the right eye, and the lateral direction of the visual line of the right eye to the distant object is precisely determined. Next, a dark red glass is placed over the patient's left eye. Through this he can see a red light but not the test letter. The left light is now moved until the patient states that it is directly under the distant letter. He is now seeing the test letter with his right eye, which cannot see the red light. His left eye sees the red light but not the test letter. The examiner extinguishes the left light by pressing the flash button, and the patient is asked to look steadily at the test letter. This permits his deviation for distance to become manifest, since the left eye is covered by the dark red glass. Then the left light is flashed on several times for only a moment and its position changed until on its first appearing the patient sees the red light superimposed on the letter. Thus the true measure of the patient's heterophoria for distance is obtained. In measurement of vertical heterophorias the same procedure is used, but the alining light is placed so that the patient sees it slightly to one side of the letter.

In measurement of a lateral heterotropia for distance by the cover test (the objective method), the left eye, for example, is covered, and the patient is directed to look with his right eye alternately at the distant test letter and at the right light. The light is moved until the right eye does not move at all laterally in looking from the test letter to the light. Since the light can be brought to a position about 0.5 arc degree below the distant test letter without

hiding it, this light movement up and down is often unobserved. Now the right light is just below the line of fixation from the right eye to the test letter. The direction of the distant test letter having been established, the right light is extinguished or moved vertically out of view. Such vertical movement still leaves the lateral direction indicated on the horizontal scale. Next the cover is moved from side to side, and the position of the left light is changed until there is no movement when the right eye, which is fixing the distant test letter, is covered and the left eye takes up fixation of the left light. The left eye is now covered, and the patient is instructed to concentrate on the distant test letter. This permits any heterophoria or heterotropia for distance to become manifest. After a few moments the cover is suddenly shifted to the right eye, and any movement of the left eye as it again fixes the left light is noted. If movement is noted, the left light is adjusted in a direction to neutralize it, and the last part of the procedure is repeated until no motion of the left eye is observed. While the cover is being alternated from one eye to the other, any movement of the eye which is fixing the distant test letter may be disregarded, since the angle of the visual line between the right eye and the test letter has already been determined. When the change from fixation of the distant test letter with the right eye to fixation of the left light with the left eye causes no movement of the left eye, the heterophoria, or squint, for distance is read directly on the differential scale.

In measuring the vertical deviation for distance the same method is used, but the light for the right eye is alined just beside the visual line instead of just beneath it. The light is then moved laterally out of view without the reading on the vertical scale being disturbed. The motion of the left eye is stopped by changing the position of the left light. When the movement is neutralized, the difference between the readings on the two vertical scales indicates the degree of vertical heterophoria, or squint, which exists.

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# HYDROGEN ION CONCENTRATION OF THE VITREOUS IN THE LIVING EYE

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The concept of the relation of even small changes in the hydrogen ion concentration to vital biochemical and biophysical processes has stimulated many studies on the acid-base equilibrium in various body fluids and tissues. The interest of ophthalmologists has been focused mainly on one phase of this relation, that is, the changes in the turgescence of colloids due to a shift in the hydrogen ion concentration. Its possible bearing on the problem of glaucoma was considered by Fischer [1] and was later the basis for experimental work on the $p_H$ volume curve of the vitreous (Baurmann and Thiessen,[2] Duke-Elder,[3] Goedbloed,[4] Salit and O'Brien,[5] von Sallmann [6] and others). No experimental work in ophthalmology, however, has been reported on the relation of the $p_H$ of the milieu to the optimal action of various enzymes, such as tissue proteinases (cathepsin and peptidases) and the proteolytic enzymes in polymorphonuclear leukocytes and clasmatocytes, whereas in other fields of medicine the problems of inflammation, autolysis and necrosis have been studied from this viewpoint (Bradley,[7] Schade and associates,[8] Menkin and associate,[9] Lurie,[10] Hagemann,[11] Steinberg and Dietz,[12] Bayerle and Borger [13] and others). These studies have shown that accurate knowledge of the hydrogen ion concentration is of major importance in physiologic, as well as clinical, problems.

A considerable number of reports have been made on determinations of the $p_H$ of the vitreous in experimental animals, and in a few instances in the human eye, but all the studies have been carried out on vitreous fluid removed from the eyes or on enucleated globes. As early as 1925, studies were conducted on the actual reaction of the vitreous fluid of the human eye with

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reference to glaucoma (Gala [14]), but in this investigation, as well as in the early experimental work on rabbits (Scalinci [15]), the technic was crude, as the loss of carbon dioxide was not prevented prior to the determination, the temperature factor was neglected and a colorimetric method was applied. Most of the later investigators tried to eliminate the error due to the uncontrolled loss of carbon dioxide by covering the removed vitreous with paraffin oil (Tria and de Simone,[16] Adams and Kerridge,[17] de Rosa,[18] Salit [19] and others). The studies on the rabbit vitreous usually were carried out a short time after the death of the animal, but several hours were lost between the determination of the $p_H$ of the vitreous of cattle and their slaughter (Salit,[19] Goedbloed,[4] Redslob [20]). The small number of experiments reported by the various authors further increased the difficulty in evaluation of the results. Only Salit's investigations on the vitreous of cattle and the studies of Oyama [21] on the vitreous of rabbits presented a sufficient number of experiments. As the technic of Oyama seems the least open to criticism from the point of view of determination of the physiologic $p_H$, it will be briefly discussed. Oyama withdrew the vitreous from the living eye of the unanesthetized rabbit into a syringe which was used as a hydrogen electrode and determined the electromotive force at a temperature of 38 C. As possible errors in the method the author mentioned the escape of carbon dioxide from the vitreous fluid into the hydrogen atmosphere of the electrode and the lowering of the partial pressure of the hydrogen gas by the escaping carbon dioxide. In addition, the filling of the needle with a small amount of a solution of sodium chloride of unknown $p_H$ hydrogen ion concentration and the disadvantages of the hydrogen electrode, as summarized by Dole,[22] must be considered in judging the readings obtained by Oyama. The hydrogen electrode was also used by Kodama,[23] Tria and de Simone [16] and de Rosa,[18] but under less favorable conditions. Redslob [20] employed an antimony electrode in a few instances and Mayer [24] a gold electrode. Gala,[14] Scalinci [15] and Salit [19] utilized colorimetric methods.

Adams and Kerridge [17] were the first to apply a glass electrode to rabbit vitreous (3 experiments). It would exceed the purpose of this paper to enumerate the many advantages of the glass electrode for such determinations; the interested reader is referred to the standard text by Dole,[22] who cited, among others, the following advantages:

> [1] The glass electrode comes to equilibrium immediately, allowing $p_H$ measurements to be made with great rapidity. [2] The glass electrode can be inserted and the $p_H$ measured without changing the $p_H$ of the solution and without changing the solubility of gases such as carbon dioxide. . . . [3] The glass electrode has no salt or protein error.

These qualities made the glass electrode suitable for the measurement of the $p_H$ in vivo in various tissues and in different parts of the body. Voegtlin, Kahler and associates [25] (1932-1938) studied extensively the applicability of a new capillary glass electrode and described a technic for measuring the $p_H$ of normal and malignant tissues. They also investigated the effect of the intraperitoneal injection of dextrose and fructose and the influence of severe depression of the respiration on the hydrogen ion concentration of voluntary mammalian muscle. In 1934 Ball [26] used

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a capillary glass electrode of a spear type for determination of the $p_H$ of the intestinal wall of the white rat. Dubuisson [27] (1936-1937) recorded the changes in the $p_H$ which occur in the muscle during action. Dusser de Barenne, McCulloch and Nims [28] (1937) measured the $p_H$ of the cerebral cortex with a glass electrode of thin membrane type. A technic similar to that described by Voegtlin, Kahler and Fitch [25b] served Beck, Musser, Carr and Krantz [29] (1938) for the measurement of the $p_H$ of skeletal muscle and of Walker sarcoma and for the study of the effect of certain sugars on the hydrogen ion concentration of the tissue examined. Maison, Orth and Lemmer [30] (1938) reported the changes in the hydrogen ion concentration of rabbit and human striated muscle after contraction. Steinberg and Dietz,[12] in the same year, made use of the glass electrode in an investigation of the hydrogen ion concentration in relation to cell types in the inflammatory exudate of the peritoneal cavity. Blank,[31] in 1939, applied a thin membrane glass electrode to determine the $p_H$ of the skin surface. According to Dole,[22] Nungester and Kempf (1941) measured the $p_H$ of normal and pneumonic lung tissue with a penetrating glass electrode.

In application of the glass electrode for recording the $p_H$ in various parts of the body, the following disadvantages have been found: First, the friction between the electrode and the tissue caused by any slight motion may modify the reading; second, the injury of the tissue may cause a drift of potential for a certain length of time, and, third, the possible covering of the measuring membrane or capillary with blood may result in a decrease of the $p_H$. Since these disadvantages are nearly eliminated by the semifluid consistency of the vitreous and its peculiar anatomy, this part of the eye seems excellently suited to the use of such an electrode. Among the glass electrodes designed for the work on animals, the capillary electrode of Voegtlin and Kahler [25a] and the thin membrane electrode of MacInnes and Dole [32] were most satisfactory. Since the latter type of electrode permitted the measurement in a small circumscribed area of about 1 mm. in diameter, a modification of this type was made and tested for the present work in the laboratory. By means of such an electrode it was found possible to measure the $p_H$ of the vitreous of rabbits in situ and in vivo.

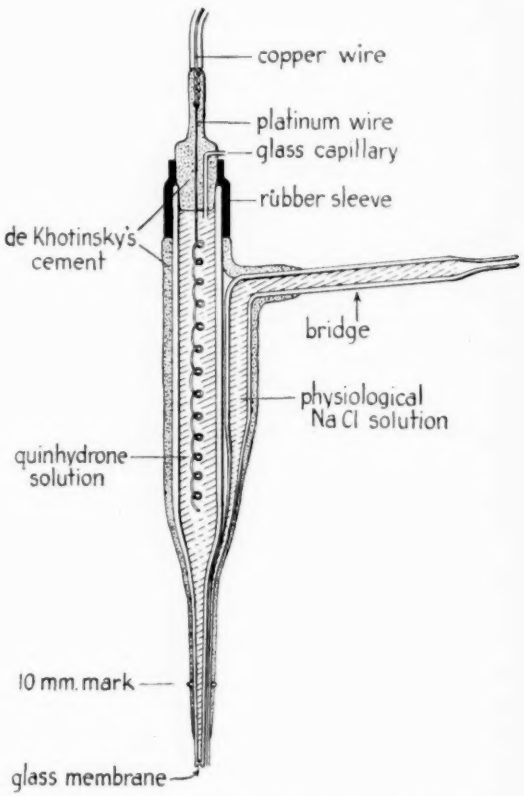


Diagram of the glass electrode which I used.

## PRESENT INVESTIGATION

*Preparation of Electrodes.*—The electrodes consisted of a tube of soft glass, one end of which was drawn out to an external diameter of 1 to 1.5 mm. (figure). A thin membrane of electrode glass (Corning 015) was then welded to the fine end of the shank, according to the technic of Nims.[33] The diameter of the measuring, concave membrane was about 0.5 mm. To obtain the connection to the reference electrode, a glass bridge was drawn to a fine capillary, bent to the surface of the supporting tube and fixed to the latter by a layer of de Khotinsky cement. This insulating material covered the electrode from its tip to its upper end to pre-

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vent the interference by a deviation film. The openings of the capillary bridge and the measuring membrane were close to each other. A saturated solution of quinhydrone and platinum were used as the inner electrode; the platinum wire was fixed in a stopper of de Khotinsky cement, which fitted into a short rubber sleeve covering the upper end of the supporting tube. A fine opening in the cement stopper provided an air vent as a safeguard against pressure on the measuring membrane. The bridge was filled with isotonic solution of sodium chloride or of three chlorides U. S. P. to connect it with a container of the same solution, in which was immersed the calomel reference electrode. The glass electrode was held by a hard rubber clamp, which could be freely moved in various directions by a series of joints. The grounded reference electrode was held in place by a simple hard rubber clamp. The cell measured was:

Pt; $Q.Q.H_2$ | N/10 HCl | Glass | Vitr. | NaCl iso.sol. || KCl sat.sol. | HgCl | Hg. ($Q.Q.H_2$ indicates quinhydrone.)

Leads to a Beckman $p_H$ meter, laboratory model G, with a temperature compensator, consisted of shielded, grounded cables suspended freely in the air. The electrode assembly was arranged in an electrically shielded, grounded cage, which also contained an insulated board for the experimental animal. The potentiometer rested on a separate table and was likewise shielded and grounded to avoid the influence of extraneous electric currents. A great number of glass electrodes (several hundred) were made. After being boiled for several hours and ripened to reduce the asymmetry potential, the electrodes which gave a linear graph with three standard buffers and had a low zero correction were selected. They were recalibrated before use. A series of experiments were carried out to study the influence of the depth of immersion. It was found that the readings did not vary when the electrode was immersed in the buffer solution from 1 to 10 mm.

*Technic of the Experiments.*—Mature chinchilla rabbits, receiving a diet of oats and hay, were given intraperitoneal injections of sodium pentobarbital, 40 mg. per kilogram, or dial with ethyl carbamate,[33a] 1 cc. per kilogram of body weight. The conjunctiva was incised a few millimeters above the limbus and the sclera exposed. The superior rectus and superior oblique muscles were resected, and the suture holding the muscle stump at the sclera was used to rotate the eye downward. An opening of 1.5 to 2 mm. in diameter was made in the sclera 6 to 8 mm. from the limbus. The bulging uvea was usually incised after the animal had been placed in the shielded cage and the electrode placed in position for its immediate insertion. The introduced electrode almost filled the opening and prevented the escape of vitreous. Measurements were made at various depths in the vitreous, i. e., at varying distances from the retina. Readings of the $p_H$ were recorded three to fifteen minutes after insertion of the electrodes, with the temperature compensator set at 37, 38 and 39 C. Immediately after the withdrawal of the electrode, the temperature of the vitreous was measured with a microthermometer, and in the later experiments, with a thermocouple, the wires of which were coated for the terminal 3 cm., except for the measuring tip, with a layer of de Khotinsky cement to obtain the necessary rigidity. The tip of the thermocouple was placed in the vitreous at the same depth as the measuring membrane of the electrode. Readings were taken on the potentiometer with standard buffer solutions before and after each experiment at 37 or 38 C., the setup of the experiments being always the same. The results of experiments were tabulated only when the readings on the standard buffers after the experiment were almost exactly the same as the readings before the experiment, a slight variation of 0.02 $p_H$ unit being allowed. The tip of the electrode and the bridge capillary were examined for traces of blood after their removal, and the eyes were dissected and examined for lesions of the lens or inner membranes and for the presence of blood in the vitreous.

33a. Each cubic centimeter of the anesthetic contained 0.1 Gm. diallylbarbituric acid, 0.4 Gm. ethyl carbamate, 0.4 Gm. monoethylurea and distilled water, to make 1 cc.

## RESULTS

*Normal Eyes.*—In 12 instances the readings for both eyes of normal chinchilla rabbits could be used (table). The results were in close agreement; the difference between comparable figures for the two eyes did not exceed 0.03 $p_H$ unit except in 2 instances in which the differences were 0.05 and 0.06 $p_H$ unit respectively. The values recorded for the $p_H$ varied from 7 to 7.1, the average $p_H$ being 7.04 at a depth of immersion of 5 to 7 mm. In the calculated average were included the results for 7 additional normal eyes, in which the fellow eye was not suitable for determinations of the $p_H$ because of previous use or accidents during the procedure. The $p_H$ values remained constant during the experiment, that is, for a period of fifteen minutes. Further measurements were recorded at the greater depth of 10 to 12 mm. from the sclera, that is, closer to the retina. The accurate loca-

*Values for the $p_H$ of the Vitreous of Normal Rabbits*

| Rabbit No. | Values for $p_H$: With Electrode Introduced to Depth of from 5 to 7 Mm. — Right Eye | Left Eye | With Electrode Introduced to Depth of from 10 to 12 Mm.* — Right Eye | Left Eye |
|---|---|---|---|---|
| 1 | 7.06 | 7.03 | 7.22 (C) | 6.82 (B) |
| 2 | 7.00 | 7.01 | 6.81 (B) | 6.78 (B) |
| 3 | 7.07 | 7.08 | 7.01 | 6.95 |
| 4 | 7.01 | 7.00 | 7.04 (C) | 6.99 |
| 5 | 7.00 | 7.00 | 6.90 | 7.07 (C) |
| 6 | 7.05 | 7.00 | 7.00 | 6.91 |
| 7 | 7.08 | 7.07 | 7.06 | 7.27 (C) |
| 8 | 7.01 | 7.03 | 7.05 (D) | 7.03 (A) |
| 9 | 7.04 | 7.04 | | |
| 10 | 7.01 | 7.00 | 7.01 (A) | 7.1-7.2 (C) |
| 11 | 7.05 | 7.03 | | |
| 12 | 7.1 | 7.04 | 7.06 | 7.04 (A) |
| 13 | 7.1 | | | |
| 14 | .... | 7.00 | .... | 7.04 (D) |
| 15 | .... | 7.05 | .... | 7.01 |
| 16 | 7.01 | .... | 7.12 (C) | |
| 17 | .... | 7.06 | .... | 7.04 |
| 18 | 7.07 | .... | 7.02 | |

* In the table, A indicates no difference between readings at different depths; B, injury potential; C, interference by hemorrhages, and D, more alkaline readings at greater depths.

tion of the electrode tip with reference to the lens and retina could not be controlled. In this position of the electrode a slight shift of the $p_H$ to the acid side, with a range of 0.01 to 0.13 $p_H$ unit, was noted in 11 eyes, the average shift being 0.054 $p_H$ unit. In 3 eyes such a shift was not evident (*A*). In 3 eyes in which readings indicating a shift to the acid side, $p_H$ 6.78 to 6.82, were obtained with the deeply introduced electrode, a lesion of the retina or of the lens was observed on dissection of the globe, and therefore these readings may be considered as indicative of injury potentials (*B*). On the other hand, in 6 eyes for which the readings of the $p_H$ at the greater depth were 7.04 to 7.27, hemorrhages in the cortical area of the vitreous were noted or traces of blood were observed on the measuring membrane or in the opening of the bridge capillary (*C*). The readings indicating slightly greater alkalinity with the deeper position of the electrode in 2 eyes (*D*) remained unexplained, since no traces of blood were noticed in the cortical part of the vitreous after dissection of the globes or on the tip of the electrode. Under the experimental conditions the temperature as measured by the thermocouple at depths of 5 to 12 mm. showed a gradient in which 1 mm. of immersion corresponded roughly to 0.1 degree C.; that is, at a depth of 5 mm. the temperature was about 0.5 degree C. less than the temperature at a depth of 10 mm.

*Comment.*—The use of the glass electrode in the form selected eliminated the main error in determination of the $p_H$ of the vitreous, namely, the loss of carbon dioxide prior to or during the procedure, since the shank of the electrode sufficiently blocked the opening in the sclera and the inner membranes. The temperature could also be evaluated much better by this means than by the methods applied by the aforementioned authors. The technic of determination of the $p_H$ as applied to the vitreous of the living animals permitted readings at circumscribed areas within the cavity, providing information unobtainable by previously described methods.

The main objections to the technic used in the present experiments lay in the necessity for general anesthesia, the slight uncertainty of the temperature factor and the unavoidable introduction of a dilute saline bridge. A bridge filled with isotonic solution of sodium chloride or of three chlorides U. S. P. was used by Voegtlin, Kahler and Fitch,[25d] as well as by other authors, in in vivo determinations of the $p_H$. It is accepted that the difference produced by this arrangement as compared with the results of in vitro determinations is slight, less than 0.02 $p_H$ unit if the electrode system is carefully calibrated with known standard buffer solutions under the same conditions of temperature as exist during the experiment. Nims [33] pointed out that the different values for any changes which occur during the course of such experiments can be ascertained within a few thousandths of a $p_H$ unit. The question whether the anesthetic agent, dial or pentobarbital, used in these investigations changed the $p_H$ of the tissue cannot be answered on the basis of the present experiments. All previous experiments in vivo were carried out in this way, with general anesthesia. It has been assumed by various investigators that an anesthesia of moderate degree induced with barbiturates has little influence on the $p_H$ of the tissue or blood (Voegtlin and associates,[25] Dubuisson,[27] Dusser de Barenne and associates,[28] Beck and co-workers,[29] Maison and associates,[30] Nims,[33] Steinberg and Dietz [12]). It would be of advantage if the temperature of the cage in which the animal is placed could be kept constant at 37 to 38 C. The insertion of the small, insulated shank of the electrode may lower the temperature a little, as may the introduction of the thermocouple wire. But it is safe to assume that these errors are small, since the electrode was immersed prior to the experiment in a buffer solution at 38 C. The complicated character of the measuring system makes one cautious, however, in the statement that the readings obtained present the true physiologic $p_H$ of the rabbit vitreous. Nevertheless, it seems that with this method fewer errors occurred than with methods used by previous authors.

The readings of the $p_H$ recorded in the present study compare most closely to the values obtained for the vitreous of rabbits by Tria and de Simone [16] (7.01) and Kodama [23] (7.1). They are similar, also, to the values for the $p_H$ of 7.09 to 7.2 determined by Schade and associates [8] for normal tissue, as against an average value of 7.35 for the blood. They deviate considerably from the values obtained by Oyama [21] and other authors. Oyama stated that a $p_H$ of 7.416 was physiologic for the vitreous of albino rabbits. It remains to be seen whether the technic applied, the breed of experimental animals or the diet on which they were kept can explain the difference in results.

The slightly less alkalinity often noted on deeper immersions of the electrode, that is, to a depth of from 10 to 12 mm., indicates nothing more than a trend toward a more acid reaction

at the cortex of the vitreous. It is not improbable that the high glycolytic activity of the retina, with the production of lactic acid, as discovered by Warburg, Posener and Negelein,[34] is related to these values for the $p_H$ near the retinal surface. Adler [35] described a decline in the sugar concentration in the posterior layers of the vitreous as compared with the concentration in the anterior layers. The glycolysis of the lens, as studied by Kronfeld [36] and others, may also play a part in establishing an increased hydrogen ion concentration in the vitreous and a slight acid drift in the cortical region of the latter. Determinations of the $p_H$ in well defined parts of the vitreous chamber by the technic described, however, were not accurate enough to permit convincing conclusions. The precise location of the tip of the electrode and its topical promixity to the retina or lens by means of ophthalmoscopic inspection was not possible, since the lower lid covered the cornea of the downward-rotated globe.

*Pathologic Conditions.*—It is not known to what extent changes in the $p_H$ of the vitreous space occur under pathologic conditions. The following series of experiments present a first attempt to study in vivo the shift of the $p_H$ in eyes with an inflammatory process of bacterial origin in the early and late stages and in eyes in which the retina was destroyed in part by the systemic use of iodates. A few observations were made on globes with experimental secondary glaucoma. They were not conclusive enough to be reported.

Inflammation was produced by the intravitreal injection of 0.05 cc. of a twenty-four hour broth culture of a mannitol-positive strain of Staphylococcus aureus in a dilution of $10^{-4}$. The injected material gave a $p_H$ of 7.85. The $p_H$ of the vitreous was measured from twenty-four hours to three months after injection of the infective organisms. The technic employed was the same as that used in normal eyes, with the electrode immersed to a depth of from 5 to 8 mm. After the measurement of the actual reaction and of the temperature of the vitreous in the same area, a small amount of vitreous fluid was withdrawn, and smears were made and stained with Giemsa's or Wright's solution for cytologic examination. In some instances the globes were removed and embedded for further histologic examination. The incidence of disturbing hemorrhages or injuries to the inner structures of the eye was higher in the later stages, especially in greatly shrunken globes.

Local acidosis was observed in all inflamed eyes. Twenty-four hours after the injection (4 eyes), the $p_H$ value reached 5.7 in one eye and ranged from 6.33 to 6.35 in 3 other eyes. During the following weeks the acidosis declined slightly to an average $p_H$ of 6.62 (7 eyes). Of 6 eyes in which the infection had been arrested by penicillin therapy and the clinical signs of inflammation had subsided, the $p_H$ readings returned to a normal range in 3 (7, 6.98 and 7.01) and declined to values indicating greater alkalinity in the other 3 (7.16, 7.19 and 7.22).

In the first days after the infection large numbers of cocci were seen in the smears or in the sections, and the inflammatory cells consisted almost exclusively of polymorphonuclear leukocytes. In later stages numerous macrophages were present, and the polymorphonuclear leukocytes displayed various stages of degeneration. A distinct relation between the cell type and the hydrogen ion concentration could not be established beyond the fact that maximal acidosis was recorded in the acute, early stages, when polymorphonuclear leukocytes were predominant. Further experiments are necessary to determine whether this initial acidosis is due to acid formation resulting from bacterial metabolism.

The acidity of the vitreous measured in the first weeks after the infection exceeded that observed by Steinberg and Dietz [12] in the peritoneal exudate of rats produced by staphylococcic infections, with $p_H$ readings of 6.6 to 7.27. This range presents only a slight change as compared with the values determined for normal rats, in which a concentration of hydrogen ions of from 6.87 to 7.1 was recorded. The relatively great variations of the physiologic values for the $p_H$ in the peritoneal cavity suggest, however, that the unknown placing of the tip of the electrode in the abdomen, the movement of the intestine, and possibly some concealed small hemorrhages, induced potential errors which could be avoided in the intravitreal measurements on rabbits.

34. Warburg, O.; Posener, K., and Negelein, E.: Ueber den Stoffwechsel der Carcinomzelle, Biochem. Ztschr. **152**:309, 1924. Warburg, O.: The Metabolism of Carcinoma Cells, J. Cancer Research **9**:148, 1925; Die Milchsäurebildung beim Wachstum, Biochem. Ztschr. **160**:307, 1925.

35. Adler, F. H.: An Investigation of the Sugar Content of the Ocular Fluids Under Normal and Abnormal Conditions and the Glycolytic Activity of the Tissues of the Eye, Tr. Am. Ophth. Soc. **28**:307, 1930; The Metabolism of the Retina: Further Notes, Arch. Ophth. **6**:901 (Dec.) 1931.

36. Kronfeld, P.: Zur Frage der Linsenatmung, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **46**:230, 1927.

Neither Steinberg and Dietz [12] nor Lurie [10] noted a correlation between the hydrogen ion concentration of an exudate and the leukocytic formula in their experiments on rats, rabbits and dogs. Contrary to the observations of these investigators, Menkin and associates [9] had previously concluded from their extensive studies on dogs that "the cellular composition of an inflammatory exudate is a function of the concentration of the hydrogen ion in the area of inflammation." The $p_H$ concentration of a pleural exudate shifts, according to Menkin, from the alkaline to the acid $p_H$ side after two or three days. Collateral with this change is the percental fall of polymorphonuclear leukocytes and the percental rise of mononuclear phagocytes. These observations of Menkin and associates were not corroborated by the results of the present study on one type of bacterial inflammation in the rabbit vitreous.

Schimmel and Riehm [37] observed, as an apparently isolated severe injury to the retina, acute pigmentary degeneration in patients who had been treated systemically with concentrated Pregl's solution of the sodium salt of hydriodic acid and iodic acid with iodine (0.04 per cent). Riehm [38] presented experimental proof of the toxic action of concentrated Pregl's solution on the retina of rabbits. In the period following these publications the nature of this destruction was repeatedly studied. Vito,[39] Kalt [40] and, later, Sorsby [41] found that sodium iodate ($NaIO_3$) was as effective as sodium hypoiodite (NaIO), which I [42] concluded was the active principle in the concentrated Pregl solution. Because of the simpler technic, sodium iodate was used in the present experiments in order to obtain extensive destruction of the retina without primary interference with the retinal circulation.

Three injections of the aqueous solution, each of 0.03 Gm. per kilogram of body weight, were administered subcutaneously to 4 rabbits at intervals of three days. Determination of the $p_H$ was carried out from four weeks to four months after the first injection of the iodate solution. Two of the 8 eyes with the characteristic lesion fully developed could not be used for recording of the $p_H$ values, in 1 instance because of injury to the lens with the electrode, and in the other because of the death of the animal before the readings on the second eye were completed. After the measurements the remaining 6 globes were enucleated for histologic examination. The average for the $p_H$ values for the vitreous of the diseased eyes showed a decline in the hydrogen ion concentration as compared with the average for the $p_H$ values of normal rabbit vitreous. For 3 eyes the readings were within a normal range (7.1, 7.06 and 7.07); the other 3 eyes showed a shift to the alkaline side (7.4, 7.18 and 7.25). The histologic examination suggested a relation between the extent of the retinal atrophy and the alkalinity of the vitreous so far as the more alkaline readings were obtained for the vitreous of eyes with larger areas of completely atrophic retina without any other microscopically detectable lesions. Adler [35] produced atrophy of the retina in 3 eyes of rabbits by section of the optic nerve back of the eyeball and observed that the sugar content of the vitreous of the eyes operated on was much above normal. He saw the most likely explanation of this observation in the reduction of the glycolysis of the atrophied retina. It is possible that the slight shift of the $p_H$ to the alkaline side in the present experiments was also caused by interference with the glycolytic activity of the diseased retina and diminished formation of lactic acid. The possibility cannot be excluded, however, that the general condition of the experimental animal in this type of intoxication also influences the $p_H$ of the tissue.

37. Schimmel: Zur Septojodbehandlung, München. med. Wchnschr. **73**:590, 1926. Riehm, W.: Augenschädigungen nach Septojodinjektionen, ibid. **73**:590, 1926.

38. Riehm, W.: Ueber Presojod Schädigung des Auges, Klin. Monatsbl. f. Augenh. **78**:87, 1927.

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41. Sorsby, A.: Experimental Pigmentary Degeneration of the Retina by Sodium Iodate, Brit. J. Ophth. **25**:58, 1941.

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## SUMMARY

1. A glass electrode of the thin membrane type (MacInnes and Dole) was designed for determination of the $p_H$ in circumscribed areas of the vitreous in vivo. Accurate measurements of the temperature in the examined area, necessary for evaluation of the $p_H$ readings, were obtained by the use of a thermocouple.

2. The potentiometric readings of the $p_H$ of the two eyes of individual rabbits were in good agreement. A range in $p_H$ of 7 to 7.10 was recorded as the value for the normal vitreous

of rabbits. Measurements carried out in closer proximity to the retina showed in the majority of the eyes a trend toward an increase of the hydrogen ion concentration in the cortical layers of the vitreous. This shift may be the result of acid formation caused by the high glycolytic activity of the retina.

3. Local acidosis, up to a $p_H$ of 5.7, developed in the early stages of an acute staphylococcic infection of the vitreous. The acidity decreased during the following weeks. Several months after the inflammation had been arrested by penicillin therapy, a normal range of the $p_H$ was restored in the vitreous or the acidity was succeeded by a slight alkalosis.

4. In eyes in which the retina had been partially destroyed by systemic treatment with sodium iodate, readings indicated a higher alkalinity than for normal eyes.

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# AFTER-IMAGE PERIMETRY

## A RAPID METHOD OF OBTAINING VISUAL FIELDS; PRELIMINARY REPORT

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The phenomenon of after-image has long been known and studied, but it has apparently not been utilized as a means of perimetry. It is reasonable to suppose that if an after-image were produced in a patient with a lesion of the central optic pathways, there might be a defect in the after-image corresponding to the site and size of the area of damage of the visual system. This hypothesis was tested according to the following technic.

### METHOD

*Technic.*—The instrument used consists of a portable flood lamp with a 500 watt bulb and a 16 inch (40 cm.) reflector. Over the reflector is placed a translucent cover 0.5 mm. in thickness, made of two layers of white broadcloth, on the surface of which a standard visual field design is sewed in black, the lines being 5 mm. in width. The test is best carried out in a dark room with black or dark gray walls. This screen flood lamp is placed 20 cm. directly in front of the eye to be tested, the other eye being covered with a shield. At a distance of 20 cm. this 40 cm., round design represents 45 degrees of the complete visual field, being slightly smaller than the field charted as normal for a 5 mm. object at a distance of 2 meters by the standard tangent screen method. With the room lights on, the patient is asked to look at the central focal point on the design and is cautioned against blinking the eye, and the flood lamp is turned on as the ceiling lights in the room are simultaneously turned off. The flood lamp is snapped off after a one second exposure, the room being left in total darkness, and the lamp is removed from in front of the patient. Soon an after-image appears, representing 45 degrees of the patient's field of vision. With the room dark, the patient perceives a positive after-image of the design, which is an exact reproduction of the white disk with black lines. The positive after-image tends to come and go, becoming fainter with each return. The patient is allowed to study the positive after-image through three or four cycles, and then the room lights are switched on and the retina restimulated. The design is immediately reproduced as a negative after-image, which the patient perceives as a design of white lines projected on the black background. This negative after-image fades rapidly, but by means of the room lights being switched off and on the after-image is each time reproduced clearly. The patient is thus enabled to study his own "visual field." A normal eye perceives the entire design, with clearcut borders, whereas the eye with an absolute field defect perceives a distinct absence in the after-image. After studying the positive and negative after-images for approximately two minutes, the patient is able to chart his own "visual field" on a standard form, outlining any area which was not visualized in the after-image. A "control" is afforded by the use of a design with two small defects in one of the radial lines, which the patient is able to identify in the after-image.

*Results.*—A series of 50 patients, 25 with normal fields and 25 with abnormal fields, were examined by this method and the results compared with their fields obtained by the standard tangent screen method used at the Neurological Institute of New York. All the normal subjects in this series were able to see their visual fields represented by the after-image clearly, distinctly and without question. Each subject with abnormal visual fields in the series was immediately aware of his own field defect, provided the defect was absolute and not relative, and was able to chart his own fields, which corresponded closely to the fields charted by the tangent screen method. The average time required for the patient to obtain and chart visual fields for both eyes by this method was four minutes. The fields charted by this group approximated their true fields closely enough to justify the clinical use of this method. In figures 2, 3 and 4 are shown the visual fields of 3 patients, with large field defects, scotomas and enlarged blindspots due to papilledema respectively. The tangent screen fields were obtained with a 5 and a 2 mm. object on a 1 meter screen at a distance of 1 meter, with daylight illumination. The fields are charted on a 25 degree design, though they actually represent 45 degrees.

### COMMENT

The advantages of this method of obtaining visual fields are as follows:

1. The method is not tiring to the patient or to the examiner.

2. The patient is unable to look away from the fixation point, since the after-image moves simultaneously with any shift of the eye.

3. With a hand lamp the method is readily adaptable to the bed patient, who sees the after-images on the ceiling.

4. With a simple design of an object in each quadrant, the method can be utilized for children, who find the phenomenon attractive.

5. Fields can be conveniently determined daily for patients with tumor of the pituitary who are receiving roentgen ray therapy, for patients with active multiple sclerosis with changing scotomas or for patients with any type of abnormal visual fields undergoing rapid change.

6. The method is time saving, enabling one technician to increase the number of fields charted from seven to seventy or more a day.

7. It is readily adapted to the physician's office.

8. It can be utilized in "processing" methods, such as routine examinations for the armed services.

9. The apparatus is simple and easily available, since it consists only of a flood lamp and a cloth shield which any seamstress can prepare overnight.

Fig. 1.—The instrument in position.

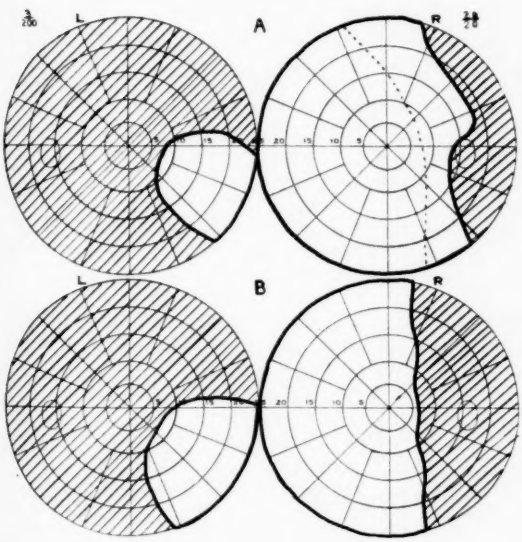


Fig. 2.—*A*, tangent screen fields and, *B*, after-image fields in a case of adenoma of the pituitary.

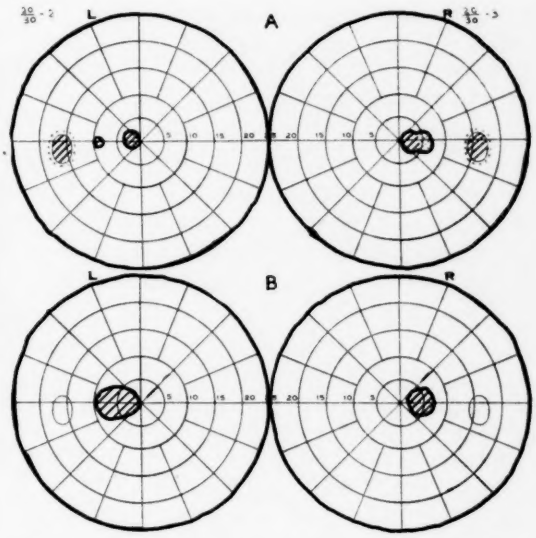


Fig. 3.—*A*, tangent screen fields and, *B*, after-image fields in a case of multiple sclerosis with scotomas.

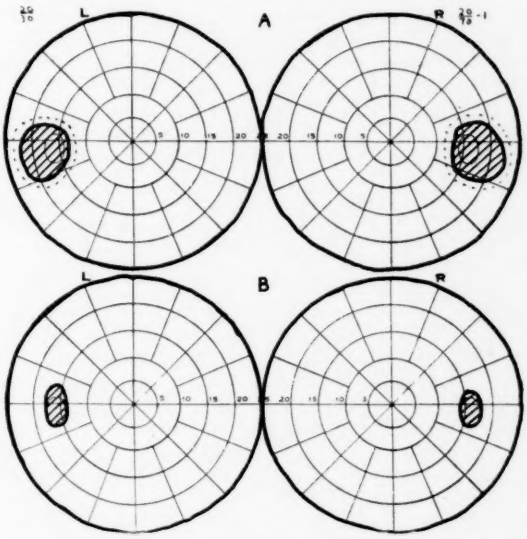


Fig. 4.—*A*, tangent screen fields and, *B*, after-image fields in a case of enlarged blindspots due to papilledema.

The disadvantages of the method are as follows:

1. The normal blindspot is not visualized, since it has no cortical representation. An enlarged blindspot, however, can be visualized in the after-image.

2. It will no doubt prove to be less accurate than the tangent screen method, though thus far it appears to be accurate enough for clinical use. This can be determined only after further study.

3. With the present technic the portion of the peripheral field tested does not represent more than 45 degrees.

4. The method reveals only absolute field defects.

SUMMARY

The value and limitations of this new method for determination of the visual fields are being thoroughly explored, and the results of the investigation will be published later.

Neurological Institute of New York.

# PENETRATION OF PENICILLIN IN RABBIT EYES WITH NORMAL, INFLAMED AND ABRADED CORNEAS

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## PENETRABILITY OF PENICILLIN

Struble and Bellows [1] pointed out that in the evaluation of any chemotherapeutic agent the efficiency of the agent depends not only on its antibacterial potency but on its diffusibility and its concentration in the infected part. Von Sallmann and Meyer [2] and Struble and Bellows [1] studied the penetration of penicillin in the normal eyes of rabbits and dogs.

Von Sallmann and Meyer [2] were unable to demonstrate any antibacterial activity of penicillin in the aqueous humor after repeated applications of solutions and ointments containing penicillin to the normal rabbit eye, but obtained high levels of penicillin in the aqueous with the corneal bath and iontophoretic technics. Struble and Bellows [1] also demonstrated high concentrations of penicillin in the aqueous humor after corneal baths of penicillin and showed that the level in the cornea exceeded the level in the aqueous when the corneal bath technic was used. Subconjunctival injections also produced high concentrations of penicillin in the cornea and aqueous humor of normal rabbit eyes, the levels in the cornea again exceeding the concentrations in the aqueous humor. The latter investigators, whose studies were, like the work of von Sallmann and Meyer, done entirely on normal eyes, did not report on the simple application of penicillin solution or ointment.

No studies on the penetration of penicillin in eyes with inflamed or abraded corneas had been reported at the time of preparation of this paper. It is in such eyes that penicillin will be used clinically. The following studies were undertaken to determine whether or not simple applications of penicillin in the form of drops or ointment to the conjunctival cul-de-sac would give satisfactory levels in the aqueous humor and thus remove the necessity of resorting to subjunctival injections, corneal baths or iontophoresis in the presence of corneal inflammation, for it is quite thinkable that the permeability of the pathologic cornea to penicillin is different from that of the normal cornea.

*Method.*—All the studies were made on rabbit eyes. The rabbits were of a brown-eyed or blue-eyed chinchilla strain, and weighed 2 to 3 Kg. each. The penicillin in solution consisted of 500 Oxford units of the sodium salt per cubic centimeter of isotonic solution of sodium chloride.[3] The penicillin ointment was prepared with a polyethylene glycol (Carbowax) base recommended by Dr. Frank Meleney through the Committee on Surgery of the National Research Council.[4] The concentration of penicillin in the ointment was 500 Oxford units per gram of base. Four drops of the penicillin solution or 0.2 Gm. of penicillin ointment was applied to the conjunctival sac once, and aqueous humor was withdrawn fifteen minutes, forty-five minutes or one hour and forty-five minutes after the instillation. The cornea and the cul-de-sac were thoroughly washed with isotonic solution of sodium chloride, and then the cornea was anesthetized with 1 to 2 drops of 0.5 per cent tetracaine hydrochloride, after which limbal punctures were made with a sterile 27 gage needle attached to a sterile tuberculin syringe. In this manner, the local anesthetic did not influence the penetration of the penicillin.

The same procedure was carried out on 24 normal rabbits, 24 rabbits with inflamed corneas and 24 rabbits with mechanically denuded corneas. Inflammation of the corneas was produced in 24 rabbits by intracorneal injections of 0.01 cc. of a twenty-four hour broth culture containing approximately 200 organisms. The organism used was Pasteurella leptiseptica, the ulcers produced by this organism having been previ-

Read at a meeting of the College of Physicians of Philadelphia, Dec. 21, 1944.

From the Department of Ophthalmology, University of Pennsylvania School of Medicine.

The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania.

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2. von Sallmann, L., and Meyer, K.: Penetration of Penicillin into the Eye, Arch. Ophth. **31**:1 (Jan.) 1944.

3. The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutics and Other Agents of the National Research Council.

4. Meleney, F. F.: Personal communication to the authors, July 17, 1944. The Carbowax compounds are polyethylene glycols of high molecular weight. The one used in these studies had a molecular weight of 4,000.

ously described.[5] The epithelium was removed from the corneas of 24 rabbits by rubbing the corneal surface with gauze, fluorescein staining serving as a guide to the amount removed. Approximately one third of each corneal surface was thus denuded.

Into 12 additional normal rabbit eyes drops of penicillin solution were instilled repeatedly every fifteen minutes for one hour. Specimens of aqueous were withdrawn from 4 eyes at each of the following intervals after the last application of penicillin: fifteen minutes, forty-five minutes and one hour and forty-five minutes.

The specimens of aqueous humor from 12 normal rabbit eyes were analyzed for concentration of penicillin at fifteen minutes, forty-five minutes and one hour and forty-five minutes after an intramuscular injection of 1,500 Oxford units of penicillin per kilogram of body weight. Four eyes were used for each time interval. The same procedure was then repeated on 12 rabbit eyes with corneal inflammations caused by intracorneal injections of Past. leptiseptica.

All concentrations of penicillin in the aqueous humor were determined by the bioassay method of Holmes and Lockwood.[6] This method was satisfactory in our hands for levels above 0.02 unit per cubic centimeter.[7] The error in this biologic method is approximately 20 per cent.

each instance. It is evident from these results that instillation of penicillin in drops or as an ointment, even when repeated four times an hour, fails to produce detectable concentrations of the substance in the aqueous of the normal rabbit eye. This confirms the observation of von Sallmann and Meyer.[2] However, definite concentrations of penicillin in the aqueous humor could be obtained after only one application of solution or ointment to rabbit eyes with inflamed or denuded corneas. All levels of penicillin in the aqueous humor of such eyes were above 0.2 Oxford unit per cubic centimeter one hour and forty-five minutes after a single instillation of either drops or ointment. From the results recorded in table 2 it is evident that intramuscularly administered penicillin does not penetrate readily into the aqueous humor of the normal rabbit eye but that it does penetrate readily into the aqueous of the rabbit eye with an inflamed cornea.

TABLE 1.—*Concentrations of Penicillin in the Aqueous Humor Obtained by Local Instillation of Penicillin in Solution and in Ointment Vehicles* *

| Time of Aqueous Humor Puncture after Instillation of Penicillin, Min. | Eyes with Normal Cornea | | | Eyes with Inflamed Cornea | | Eyes with Abraded Cornea | |
|---|---|---|---|---|---|---|---|
| | Solution, Oxford Units per Cc. | Ointment, Oxford Units per Cc. | Repeated Instillation of Solution,† Oxford Units per Cc. | Solution, Oxford Units per Cc. | Ointment, Oxford Units per Cc. | Solution, Oxford Units per Cc. | Ointment, Oxford Units per Cc. |
| 15 | 0 | 0 | 0 | 0.5 | 0.5 | 1.5 | 0.6 |
| 45 | 0 | 0 | 0 | 0.5 | 0.8 | 1.5 | 0.6 |
| 105 | 0 | 0 | 0 | 0.4 | 0.4 | 0.6 | 0.4 |

* The concentration at each time interval represents the average for 8 eyes, except for the values for repeated instillations of the solution; in these tests 4 eyes were used for each time interval.
† The instillation of the solution was repeated every fifteen minutes for four doses.

TABLE 2.—*Concentration of Penicillin in the Aqueous Humor Produced by Intramuscular Administration of 1,500 Oxford Units of Penicillin Per Kilogram of Body Weight* *

| Time of Aqueous Humor Puncture after Administration of Penicillin, Min. | Eyes with Normal Cornea, Oxford Units per Cc. | Eyes with Corneal Inflammation, Oxford Units per Cc. |
|---|---|---|
| 15 | 0 | 0.4 |
| 45 | 0 | 0.15 |
| 105 | 0 | 0.15 |

* Each concentration obtained represents the average for 4 eyes.

*Results.*—The results are tabulated in tables 1 and 2. Each value recorded represents the average for 4 or 8 eyes and is so specified in

*Comment.*—Rammelkamp and Keefer [8] showed that the concentration of penicillin in serum required for maximum bacteriostatic effect against Streptococcus haemolyticus is 0.019 unit per cubic centimeter and that 0.15 unit per cubic centimeter produces maximum bacteriostasis against Staphylococcus aureus. It is evident from the concentrations in the aqueous recorded here that this necessary antibacterial concentration is exceeded for a period of one hour and forty-five minutes after one application of solution or ointment containing penicillin in eyes with loss of the corneal epithelium barrier or with corneal infections. This indicates that repeated instillation of the drops or ointment once every two hours in such eyes would maintain adequate levels of penicillin in the aqueous humor.

Struble and Bellows [1] showed that the levels in the cornea always exceed the levels in the

5. Leopold, I. H.; Holmes, L., and LaMotte, W. O., Jr.: Local Versus Systemic Penicillin Therapy of Rabbit Corneal Ulcers Produced by Gram-Negative Rod, Arch. Ophth. **32**:193 (Sept.) 1944.

6. Holmes, L., and Lockwood, J.: Studies on Bioassay of Penicillin, Am. J. M. Sc. **207**:267 (Feb.) 1944.

7. Bioassays were done in the Harrison Department of Surgical Research, University of Pennsylvania, with the assistance of Dr. Lida F. Holmes.

8. Rammelkamp, C. H., and Keefer, C. S.: Absorption, Excretion and Distribution of Penicillin, J. Clin. Investigation **22**:425 (May) 1943.

aqueous humor when the penicillin is applied locally. They also showed that the concentration in the cornea is less than that in the aqueous humor when the penicillin is given intravenously. It follows, therefore, that the concentration of penicillin in the cornea was probably greater than that in the aqueous in each instance in the present study in which penicillin was used locally. It has been demonstrated experimentally [5] that local penicillin therapy is superior to intramuscular therapy for corneal inflammations. The present studies on penetration of penicillin also indicate that local application is superior to parenteral administration of penicillin in obtaining high concentrations in the cornea. One can conclude from these studies that it is not necessary to resort to iontophoresis or to the corneal bath technic in order to obtain satisfactory levels of penicillin in the aqueous humor when the corneas have been denuded or are infected. The simple instillation of drops of solution containing 500 Oxford units of penicillin per cubic centimeter or the application of penicillin ointment will give satisfactory levels in the aqueous humor in such eyes.

This increased intraocular penetration of locally and of parenterally administered penicillin in eyes with pathologic corneas over that observed in eyes with normal corneas has been noted similarly for the sulfonamide compounds.[9]

### EFFECTS OF THERAPEUTIC CONCENTRATIONS

It is essential to determine the local toxic effects of any new agent before recommending its repeated local use in the eye. The experiments of Florey and associates [10] on tissue cultures and the studies of Thygeson on leukocytes, cited by Hobby and associates,[11] indicated that little if any toxic effects on the corneal epithelium should be expected from penicillin. Von Sallmann,[12] however, showed that corneal baths with concentrations of 0.5 to 1 per cent of penicillin (sodium salts, $p_H$ 7 to 8) damaged the corneal epithelium and the superficial stroma. This damage of the corneal epithelium produced by high concentrations of penicillin in solution may account for the high concentration of penicillin in the aqueous humor obtained by the corneal bath technic of Struble and Bellows.[1] Von Sallmann [2] also disclosed that a concentration of 0.25 per cent of the penicillin salt produced corneal damage when applied by iontophoresis but not as a corneal bath. A concentration of 0.1 per cent of sodium penicillin produced little or no corneal damage in his hands, even when applied by iontophoresis.

Of the several factors which must be considered in determination of the toxicity of any compound to be applied locally to the eyes, the concentration of the agent and the frequency of application are important. The studies of von Sallmann [12] indicated the upper limits of concentration. The purpose of the present experiment was to determine the influence of repeated applications of a therapeutically effective concentration of penicillin on the regeneration of corneal epithelium.

*Method.*—Twelve rabbits were used in this series, all of a blue-eyed chinchilla strain and weighing between 2 and 3 Kg. The corneal epithelium was removed from the entire cornea of each of the 24 eyes. Previous experiments have shown that eyes with denudation involving the limbus are more likely to show retardation of epithelial regeneration from chemotherapeutic agents than are eyes with central denudations not involving the limbus.[13] All the eyes were anesthetized with 0.5 per cent tetracaine hydrochloride. The eyes were proptosed, and the epithelium was removed by rubbing with gauze swabs, as previously described.

Two per cent fluorescein sodium was used for staining. This acted as a guide to the extent and completeness of denudation. The sodium salt of penicillin was used in a concentration of 500 Oxford units per cubic centimeter of isotonic solution of sodium chloride. Four drops of this solution, $p_H$ 8, were applied hourly to the right eye of each rabbit. Application was started immediately after denudation had been completed. The treatment ran from 8 a. m. until 12 o'clock midnight each day. Application of penicillin was also continued for twenty-four hours after each cornea failed to stain with fluorescein. The left eye of each rabbit acted as the control and received no therapy.

TABLE 3.—*Influence of Local Applications of Penicillin on Regeneration of Corneal Epithelium*

| | Day of Regeneration | | | | | |
|---|---|---|---|---|---|---|
| | Fourth | Fifth | Sixth | Seventh | Eighth | Ninth |
| No. of control eyes healed on each day... | 2 | 1 | 2 | 3 | 1 | 3 |
| No. of penicillin-treated eyes healed on each day..... | 4 | 2 | 2 | 2 | 1 | 1 |

9. Gallardo, E., and Thompson, R.: Sulfonamide Content of Aqueous Humor Following Conjunctival Application of Drug Powders, Am. J. Ophth. **25**:1210 (Oct.) 1942. Scheie, H. G., and Leopold, I. H.: Penetration of Sulfathiazole into the Eye, Arch. Ophth. **27**:997 (May) 1942. Leopold, I. H., and Scheie, H. G.: Studies with Microcrystalline Sulfathiazole, ibid. **29**:811 (May) 1943.

10. Abraham, E. P.; Florey, H. W.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G., and Jennings, M. A.: Further Observations on Penicillin, Lancet **2**:177 (Aug. 16) 1941.

11. Hobby, G. L.; Meyer, K., and Chaffee, E.: Chemotherapeutic Activity of Penicillin, Proc. Soc. Exper. Biol. & Med. **50**:285 (June) 1942.

12. von Sallmann, L.: Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch. Ophth. **30**:426 (Oct.) 1943.

13. Adler, F. H.; Leopold, I. H., and Steele, W. H.: Unpublished data.

All the eyes were examined and stained daily. The results are recorded in table 3.

*Comment.*—It is evident from these data that local application of a solution of penicillin has no deleterious influence on the regeneration of corneal epithelium. Therefore it is safe, from this standpoint, to make repeated local instillations of the solution of penicillin in prevention and treatment of infection of the cornea.

## CONCLUSIONS

1. Penicillin in solution or in ointment fails to penetrate into the aqueous humor of the normal rabbit eye after one local instillation but penetrates readily into the anterior chamber of rabbit eyes with corneal abrasion or with corneal ulcer.

2. The concentrations obtained in the anterior chamber of the eyes with inflamed or abraded corneas after local instillation of penicillin exceed the probable therapeutic level.

3. It is not necessary to resort to iontophoresis, the corneal bath technic or subconjunctival injection in order to obtain effective concentrations of penicillin in the aqueous humor of eyes with infected corneal ulcers or corneal abrasions.

4. Instillation of a solution of penicillin (500 units per cubic centimeter of isotonic solution of sodium chloride) or penicillin ointment (500 units per gram) need be made only once every two hours to the conjunctival cul-de-sac to maintain high concentrations in the aqueous humor.

5. Repeated applications of penicillin solution (500 units per cubic centimeter of isotonic solution of sodium chloride) do not retard regeneration of corneal epithelium significantly.

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# EPIDEMIC KERATOCONJUNCTIVITIS

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Scattered epidemics of acute conjunctivitis, characteristically complicated by punctate corneal lesions, have occurred in the United States during the past few years. Since the disease first reached epidemic proportions in the shipyards on the Pacific Coast, it came to be called "shipyard conjunctivitis," or "California conjunctivitis." That it may have been present in California before it became epidemic is suggested by the fact that in 1938 Hobson [1] found 16 cases of a similar disease in a veterans' hospital at San Fernando, Calif. Rieke [2] estimated that 600 cases occurred in one shipyard in Oregon in 1941, and de Roetth,[3] at the same time, called the disease "epidemic keratoconjunctivitis" and drew attention to its association with superficial punctate keratitis. Hogan and Crawford [4] summarized the disease in a report of 125 cases from the San Francisco Bay region. It is interesting to note that in the epidemics on the Pacific Coast corneal lesions failed to develop in many cases.

In 1889 Fuchs [5] reported 38 cases of a disease he called "superficial punctate keratitis," which occurred in epidemic form in Vienna. The keratitis was preceded by acute conjunctivitis, and the disease appears to have been similar to, if not identical with, the disease now under discussion. In his description Fuchs stated that the condition was a form of superficial keratitis related to herpes of the cornea but not associated with the formation of vesicles, and that the corneal changes had a predilection for the superficial layers and were concentrated in the central portions of the cornea. He also emphasized that the disease was frequently unilateral and that after recovery from the acute condition pain, photophobia and lacrimation were common. Adler,[6] von Reuss [7] and others described a similar disease occurring in other parts of Europe at about the same time.

The next reports came from Bombay, India, where in 1900 Herbert [8] observed 26 cases of a similar disease. American physicians who visited India between 1900 and 1920 spoke of seeing a severe conjunctivitis associated with corneal opacities which was not trachoma. In 1920 Kirkpatrick [9] made a short report on the disease, and Wright,[10] and later Kirwan,[11] described extensive epidemics in Madras, India. The disease became widespread in India and China between 1920 and 1933 and occurred in India, China and Malaya from 1933 to 1936, in Germany from 1938 to 1940 and in Malaya, again, from 1935 to 1938. Hamilton,[12] in a survey of ocular disease in Tasmania, described numerous cases of a similar disease, and

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During the early part of this study convalescent serum was drawn and prepared under the supervision of Dr. J. E. Perkins and Dr. R. F. Korns, of the New York State Department of Health. The major portion of the convalescent plasma was prepared by the blood bank of the Presbyterian Hospital, under the supervision of Dr. John Scudder. Dr. Murray Sanders and Mrs. Rose Alexander tested all specimens, donors and recipients for the presence of antibodies.

1. Hobson, L. C.: Acute Epidemic Superficial Punctate Keratitis, Am. J. Ophth. **21**:1153-1155 (Oct.) 1938.

2. Rieke, F. E.: Epidemic Conjunctivitis of Presumed Virus Causation: Report of Estimated 600 Cases in One Shipyard, J. A. M. A. **119**:942-943 (July 18) 1942.

3. de Roetth, A. F.: Epidemic Keratoconjunctivitis: Superficial Punctate Keratitis, Northwest Med. **41**:246-248 (July) 1942.

4. Hogan, M. J., and Crawford, J. W.: Epidemic Keratoconjunctivitis with Review of Literature and Report of 125 Cases, Am. J. Ophth. **25**:1059-1078 (Sept.) 1942.

5. Fuchs, M.: Keratitis Punctate Superficialis, Wien. klin. Wchnschr. **2**:837-841 (Oct.) 1889.

6. Adler, H.: Ueber Keratitis subepithelialis centralis, Wien. klin. Wchnschr. **2**:713, 1889.

7. von Reuss, A.: Keratitis Maculosa, Wien. klin. Wchnschr. **2**:665, 1889.

8. Herbert, H.: Superficial Punctate Keratitis Associated with an Encapsulated Bacillus, Ophth. Rev. **20**:339-345, 1901.

9. Kirkpatrick, H.: An Epidemic of Macular Keratitis, Brit. J. Ophth. **4**:16-20 (Jan.) 1920.

10. Wright, R. E.: Superficial Punctate Keratitis, Brit. J. Ophth. **14**:257-291 (June) 1930.

11. Kirwan, E. O.: Epidemic Superficial Punctate Keratitis in Bengal, Proc. All-India Ophth. Soc. **3**:1, 1935.

12. Hamilton, J. B.: Eye Diseases Found in Tasmania: Eight Year Survey, M. J. Australia **1**:45-47 (Jan. 10) 1942.

Holmes,[13] in 1941, estimated that 10,000 cases occurred in Oahu, Hawaii. From all reports it is probable that the present epidemic in this country began in Malaya, and spread to Hawaii and then to the west coast of the United States.

### EPIDEMIOLOGIC CHARACTER OF CASES IN NEW YORK

Perkins, Korns and Westphal[14] summarized the epidemiologic character of the outbreak of epidemic keratoconjunctivitis which occurred in Schenectady, N. Y., in 1942. Their reports were based on observations in several thousand cases. The acute conjunctivitis in their series was bilateral in 56 per cent of cases, and corneal opacities developed in 85.5 per cent; in 28.4 per cent of the latter the opacities were bilateral. In 92 per cent of cases corneal opacities developed between the seventh and the twenty-third day of the disease. In examination a simple spotlight was usually employed, and it is possible that a higher incidence of opacities might have been found if the corneal microscope had been used. Even without the slit lamp, however, the incidence was much higher than that in any of the series previously reported on. The highest incidence of infection occurred in the medical dispensary, a fact suggesting that the dispensary may have been a source of contamination. In this connection, Sanders, Gulliver, Forchheimer and Alexander,[15] in a study of an outbreak of the disease in New York city, suggested that some of the patients in their series may have become infected while visiting a physician's office.

In my own experience, a number of patients have undoubtedly contracted the disease in clinics. In several instances it has been possible to trace the source of the infection beyond reasonable doubt and to determine accurately the period of incubation. In the cases in which a single exposure was known to have taken place, the period of incubation was usually from five to seven days.

Two cases were of particular interest. In the first, a physician was called one evening to remove a foreign body from the eye of a patient. Examination revealed a moderate amount of edema of the upper lid, with some chemosis and conjunctival infection. He was unable to find a foreign body, after careful search. Six days later a similar condition developed in the physician's eye, which became typical epidemic keratoconjunctivitis. Subsequent examination of his patient revealed the presence of many corneal opacities. The second case was that of an attending ophthalmologist at the Vanderbilt Clinic. He was presenting patients with conjunctivitis to a group of medical students. One patient had early epidemic keratoconjunctivitis, the diagnosis of which was obscure. Five days after the demonstration the ophthalmologist noted a foreign body sensation in his left eye. The symptoms gradually became more severe until there were considerable chemosis and edema of the upper lid. The disease then pursued the usual course, corneal opacities developing on the eighth day.

Two other incidents have been called to my attention. The first involved the use of the tonometer in the diagnosis of epidemic keratoconjunctivitis. As frequently occurs, the early diagnosis was obscure; so the intraocular tension was taken in order to rule out the possibility of acute glaucoma. The tonometer was then used with 2 other patients with chronic glaucoma, in both of whom epidemic keratoconjunctivitis developed on the fifth and sixth days respectively following the examination. The second incident involved the use of trial contact lenses and was called to my attention by Dr. F. H. Adler, of Philadelphia. In 2 patients who were given trial fittings of contact lenses epidemic keratoconjunctivitis developed on the fourth and sixth days respectively after the fittings.

In an effort to determine sources of infection, a large number of patients were questioned carefully. Most of them complained of a mild infection of the upper respiratory tract in association with the disease. In view of the common occurrence of such an infection, this association may of course be merely incidental, but it is not unlikely that ocular infections do occur from nasal droplets. The following cases are examples in point:

Miss N. was an operating room nurse in a large local hospital. She came in contact with few people. On her day off she went on a shopping tour and visited several large department stores. To her knowledge, she did not encounter any one with acute conjunctivitis. One week after her tour acute conjunctivitis developed in her left eye, which became typical epidemic keratoconjunctivitis.

Miss C. P. was a director of occupational therapy in a large hospital for chronic diseases, and her directing duties were such that she rarely came in contact with any one except the personnel of her department. She

13. Holmes, W. J.: Epidemic Infectious Conjunctivitis, Hawaii M. J. **1**:11-12 (Nov.) 1941.

14. Perkins, J. E.; Korns, R. F., and Westphal, R. S.: Epidemiology of Epidemic Keratoconjunctivitis, Am. J. Pub. Health, to be published.

15. Sanders, M.; Gulliver, F. D.; Forchheimer, L. L., and Alexander, R. C.: Epidemic Keratoconjunctivitis: Clinical and Experimental Study of Outbreak in New York City; Further Observations on Specific Relationship Between Virus and Disease, J. A. M. A. **121**:250-255 (Jan. 23) 1943.

made a train trip, and, although she did not knowingly come in contact with any persons with acute conjunctivitis, eight days later there developed an acute form of what proved subsequently to be epidemic keratoconjunctivitis.

These cases illustrate the possibility of infection either by fomites or droplets from persons who may or may not have the disease.

Throughout this study, the occurrence of foreign bodies and the sensation of a foreign body in the eyes of patients in whom the disease developed has been considered noteworthy. Some patients interpret the sensation of scratchiness as indicating that the onset was due to a foreign body, although no foreign body is subsequently seen. In reviewing the cases in which foreign bodies did occur, it seemed more likely that the patient was infected with the disease when the foreign body was removed than that the foreign body had carried the infection. The following case is of particular interest in this connection.

Mr. P., a hospital employee, reported to Vanderbilt Clinic with the complaint of something in his left eye. With the use of tetracaine anesthesia, a small foreign body was removed from the cornea. Sulfathiazole ointment was placed in the eye, and the eye was covered. The following morning the corneal abrasion had healed, and the eye appeared normal. Six days later the patient returned with acute conjunctivitis. A tentative diagnosis of epidemic keratoconjunctivitis was made and subsequently confirmed when typical corneal changes occurred.

Thus, although the cases of epidemic keratoconjunctivitis in which there had been no previous contact with either a physician's office or a clinic are much more numerous, clinics and dispensaries cannot escape incrimination as sources of transmission. It is obvious that ophthalmologists and physicians in general should give scrupulous attention to the cleanliness of their hands and instruments in treatment of this disease and should adopt the practice of using individual droppers for solutions, instead of dropper bottles. The virus isolated by Dr. Murray Sanders (see next section) survives in most of the common solutions used in ophthalmologic practice but deteriorates rapidly and loses considerable virulence when kept at room temperature for from three to six hours.

## ETIOLOGIC FACTORS

In 1942 Sanders[16] isolated a filtrable virus from scrapings of the conjunctiva of 2 patients with acute epidemic keratoconjunctivitis. He had inoculated a tissue culture with the conjunctival scrapings and had then injected the tissue culture intracerebrally into mice. The following part of this study records an attempt to confirm Sanders' work.

*Method of Study.*—Scrapings from the conjunctivas of 25 patients with epidemic keratoconjunctivitis were suspended in fluid tissue cultures consisting of serum ultrafiltrate, balanced saline solution and brain tissue of the embryo mouse. In these cultures the mouse brain maintains viability but shows little evidence of growth. The inoculated cultures were allowed to stand at room temperature for periods varying from five to ten days. The tissue and fluid were then placed in the tissue culture grinder and carefully ground until no evidence of tissue remained. Six white Swiss mice (Rockland strain) were each inoculated with ground tissue culture, 0.05 cc. being given intracerebrally and 0.15 cc. intraperitoneally, and 0.5 cc. was placed in a fresh tissue culture. The mice were examined daily for evidence of encephalitis.

Several of the 25 cultures were contaminated with pathogenic bacteria and were discarded. Inoculation of other cultures did not give rise to any symptoms in mice.

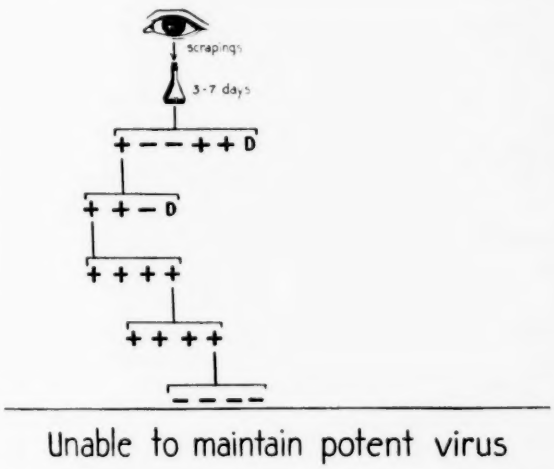


Fig. 1.—Summary of results of attempts to isolate the virus from 25 patients. Here, — indicates a healthy mouse; +, a sick mouse, and *D*, that the mouse died. Sixteen mice recovered.

Apparent takes were obtained, however, with 10 cultures. The brains of sick mice were ground and 4 or 5 healthy mice inoculated in the emulsion. Attempts to step up the potency of the virus to a concentration at which it would consistently produce death in mice failed. Figure 1 illustrates the trend of the disease. Mice recovering from inoculation with the virus which were given intracerebral injections of Sanders' virus showed a high rate of recovery as compared with the rate for the control series (table 1).

*Results.*—There is little reason to doubt that I obtained a pathogenic agent from patients with epidemic keratoconjunctivitis. It produced transient symptoms of encephalitis in mice and could be transferred by serial passage from mouse to mouse, to tissue culture and back to mice. Its potency was not increased by serial passage. Since it produced a sublethal infection, it might reasonably be expected to produce immunity.

16. Sanders, M.: Epidemic Keratoconjunctivitis: Isolation and Identification of a Filtrable Virus, J. Exper. Med. **77**:71-96 (Jan.) 1943.

To test this hypothesis, 40 recovered mice were given to Dr. Sanders. He reported as follows: "Forty mice which had survived intracerebral inoculation were given injections of stock epidemic keratoconjunctivitis virus in dilutions of $10^{-3}$, $10^{-4}$, $10^{-5}$ and $10^{-6}$. A similar number of normal mice of the same age were given injections as controls. The results (table 2) were as follows: In 40 normal mice death occurred with all dilutions. In the test animals death occurred only with dilutions of $10^{-3}$ and $10^{-4}$. No symptoms and no deaths were observed in the animals which were given intracerebral injections of the virus in dilutions of $10^{-5}$ and $10^{-6}$. This strongly suggests that the virus in your culture is similar to one isolated in this laboratory."

It seems, therefore, that the agent isolated in this laboratory may well be identical with the Sanders virus, my failure to obtain it in high concentrations accounting for the apparent differences between the two.

TABLE 1.—*Results of Injection of Sanders' Virus in Animals Recovered from Inoculation with Virus from Conjunctival Scrapings of Patients with Acute Epidemic Keratoconjunctivitis* *

| | Control Series | | | | Recovered Series | | | |
|---|---|---|---|---|---|---|---|---|
| | $10^{-3}$ | $10^{-4}$ | $10^{-5}$ | $10^{-6}$ | $10^{-3}$ | $10^{-4}$ | $10^{-5}$ | $10^{-6}$ |
| 1 | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| 2 | D + + + | + + + D | — — + + | — — — — | — — — — | — — — — | — — — — | — — — — |
| 3 | D D D | D D D | + + D D | + + — — | + + — — | D + — — | — — — — | — — — — |
| 4 | ..... | ..... | D D | D D + + | D D — — | D — — | — — — — | — — — — |
| 5 | ..... | ..... | ..... | D D | D — | — — | — — — — | — — — — |
| 6 | ..... | ..... | ..... | ..... | — | — — | — — — — | — — — — |

* In this table, and in tables 2, 3 and 4, dashes indicate a healthy mouse; plus signs, a sick mouse, and D, that the animal died.

TABLE 2.—*Results of Intracerebral Inoculation of Epidemic Keratoconjunctivitis Virus into Forty Recovered Mice*

| | Date | Dilutions of Virus | | | |
|---|---|---|---|---|---|
| | | $10^{-3}$ | $10^{-4}$ | $10^{-5}$ | $10^{-6}$ |
| First test | 6/24 | — — — — | — — — — | — — — — | — — — — |
| | 6/25 | — — — — | — — — — | — — — — | — — — — |
| | 6/28 | D D D D — | D D D — — | — — — — | — — — — |
| | 7/ 3 | — | — — | — — — — | — — — — |
| Second test | 6/29 | — — — — | — — — — | — — — — | — — — — |
| | 6/30 | — — — — | — — — — | — — — — | — — — — |
| | 7/ 2 | D — — — | — — — — | — — — — | — — — — |
| | 7/ 3 | D D D D | — — — — | — — — — | — — — — |
| | 7/ 5 | ..... | D D — — — | — — — — | — — — — |
| | 7/ 6 | ..... | D — — | — — — — | — — — — |
| | 7/13 | ..... | — — | — — — — | — — — — |
| Control | 6/29 | — — — — | — — — — | — — — — | — — — — |
| | 6/30 | — — — — | — — — — | — — — — | — — — — |
| | 7/ 2 | D D D — — | — — — — | — — — — | — — — — |
| | 7/ 3 | D D | — — — — | — — — — | — — — — |
| | 7/ 5 | ..... | D D D D D | D D — — — | — — — — |
| | 7/ 6 | ..... | ..... | D D D | D — — — — |
| | 7/ 7 | ..... | ..... | ..... | D D D D |

## THE CLINICAL DISEASE

The signs and symptoms of epidemic keratoconjunctivitis are characteristic of hyperacute conjunctivitis. The disease may be divided into three stages. Stage 1 is an acute phase, in which the primary symptoms are those of sensation of a foreign body, with moderate itching and burning. The most striking features are edema of the upper lid, chemosis and edema of the semilunar fold and caruncle. The sensation of scratchiness present during this acute phase may be so intense and of such sudden onset that the patient is sure he has a foreign body. Edema is almost always striking, especially in the bulbar conjunctiva. In some patients the chemosis is so severe that the bulbar conjunctiva is exposed even when the eye is closed. The majority of patients have moderate chemosis, associated with hyperemia of the conjunctival blood vessels. During this stage the eye frequently feels enlarged, and many patients have complained of pain and discomfort on rotation of the eyeball. This symptom may indicate changes in Tenon's capsule.

The disease enters the second stage in approximately forty-eight hours (fig. 2). Large follicles and considerable subconjunctival infiltration develop, particularly in the lower lid, but in the upper retrotarsal fold and the fornices as well. The follicles in the conjunctiva are large, translucent and usually oval. Between follicles the conjunctiva shows moderate papillary hyper-

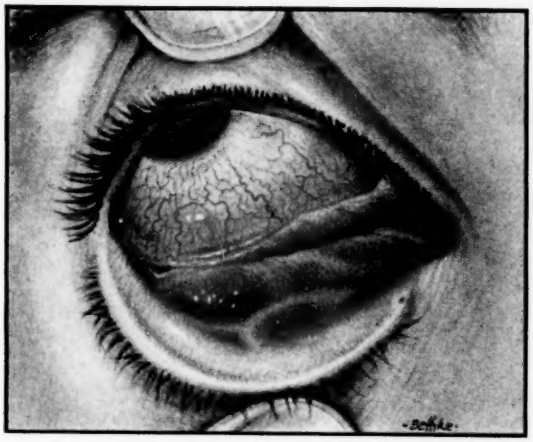

Fig. 2.—Appearance of the eye in the second stage of epidemic keratoconjunctivitis.

trophy, with considerable hyperemia. During this phase there is nearly always a palpable, slightly tender preauricular lymph node. There may also be submental and submaxillary lymphadenopathy. It is during this phase that symptoms of involvement of the upper respiratory tract are often present, with a scratchy sensation in the throat. In some patients follicular pharyngitis has occurred. During both the acute and the follicular stages of the disease, tearing is a prominent symptom, and not infrequently the tears are blood stained. After from five to six days the edema decreases. The lymphadenopathy may be gone by the sixth day or may persist for several weeks. The tenderness of the lymph nodes rarely lasts beyond the sixth day. Frequently small hemorrhages are seen on both the bulbar and the palpebral conjunctiva but are not so severe as the hemorrhages accompanying acute pneumococcic conjunctivitis.

During this phase of the disease a pseudomembrane may develop on either the upper or the lower lid. It is thin as compared with the thick pseudomembrane of streptococcic conjunctivitis, but much thicker than the fine pseudomembrane associated with allergic conjunctivitis. In 67 per cent of this series a pseudomembrane was present by the third to the fifth day. Microscopic examination of the pseudomembrane shows it to be composed almost entirely of epithelial cells with mononuclear cells scattered throughout. Early in its development the slightly opaque translucent membrane is composed almost entirely of viable superficial conjunctival cells. Later, when the membrane is light yellow (usually on the fifth to the seventh day), it contains many more mononuclear cells and degenerating epithelial cells. I was unable to demonstrate virus inclusion bodies in any appreciable number, although the Giemsa method may reveal an occasional blue-stained body in the cytoplasm. The victoria blue stain failed to demonstrate any free virus elementary bodies.

The third stage of the disease is characterized by persistence of the follicular conjunctivitis and the development of corneal changes. These changes produce symptoms of photophobia and blurring of vision. At times the blurring may be severe before any corneal opacities appear, owing to slight edema of the corneal stroma. Corneal opacities usually begin to form on the seventh or the eighth day (fig. 3). There is considerable variation in the manner in which they occur, but typically they begin as minute, discrete subepithelial dots. These dots increase in number to form opacities, approximately 1 mm. in diameter, located just beneath the epithelium and seeming to lie in or on Bowman's membrane. They are usually circular and circumscribed by a sharp border. The epithelium over the surface is occasionally slightly raised but does not stain with 1 per cent fluorescein sodium. The opacities are concentrated in the central portion of the cornea and are usually most numerous over the pupillary area. Occasionally they are so numerous that they coalesce to form a gray opacity in the superficial layers of the cornea. In spite of their numbers and their proximity, it is almost always possible with the biomicroscope to see that they are composed of discrete nebulas and that they do not all lie in the same level of the cornea, some being on Bowman's membrane and some under it. When they are numerous photophobia is usually pronounced and there is considerable loss of vision.

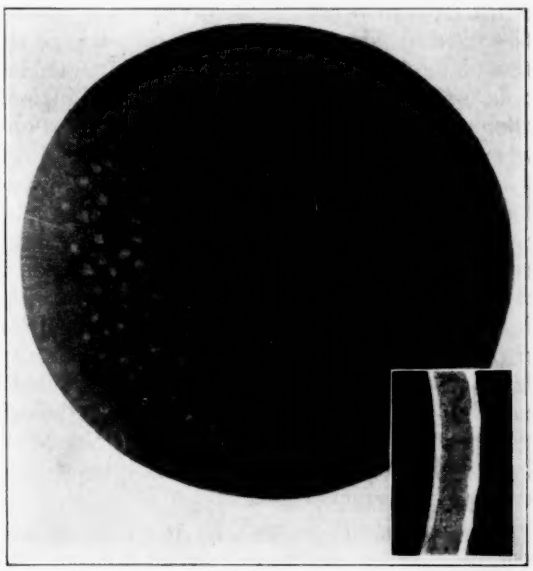

Fig. 3.—Appearance of corneal opacities in the course of epidemic keratoconjunctivitis.

The corneal opacities usually increase in number and size from the eighth to the twenty-first day, during which time the conjunctival signs are decreasing. The hyperemia gradually decreases, and the eye is white after three or four weeks. The blurring of vision and photophobia, especially in artificial light, continue for several months, and many patients complained that if they did excessive near work there was a return of mild symptoms. Several patients were followed for periods up to eighteen months. The clearing of the opacities is a gradual process. The fine dots composing the opacities decrease in number, and the density gradually decreases, with increase in visual acuity. Vision is usually normal but "fuzzy" long before the opacities have

disappeared. Many of the opacities disappear without leaving any perceptible scar. In nearly all the patients followed for a long period one or two opacities remained visible with the slit lamp. In none of the patients did permanent loss of vision result. Bedell [17] reported on the clinical observations in a large number of cases and also concluded that no permanent corneal damage results.

*Pathologic Features.*—The pathologic elements were studied in conjunctival scrapings. No biopsies of the conjunctiva were made. The conjunctival epithelial cells appeared to be normal and showed no evidence of inclusion bodies, although, as previously mentioned, blue-staining bodies were noted in the cytoplasm of a few cells. Similar bodies have been observed with other types of conjunctivitis, and their significance is as yet unknown. In general the pathologic characteristics were the same as those already described by Hogan and Crawford.[4] Large and small lymphocytes, with a few large mononuclear cells, predominated in the scrapings. Polymorphonuclear leukocytes were rarely seen, and only when there was bacterial contamination. From the character of the scrapings one would suspect that the follicle contributed many of the lymphocytes but that the entire conjunctiva was densely infiltrated with them. A striking observation in my cases was the unusual number of broken inflammatory cells. This may constitute a point of differentiation of the disease from Béal's conjunctivitis, in which lymphocytes also predominate but fragile cells are rare. The pathologic picture in mice has been discussed by Sanders.[16] In this species the Sanders virus gives rise to mild lymphocytic encephalitis.

*Bacteriologic Features.*—Early in the disease cultures were invariably sterile, while later, after considerable local medication, nonpathogenic staphylococci were almost always seen. Xerosis bacilli and other diphtheroids were recovered, and from a few patients Staphylococcus aureus was obtained. In the latter a few polymorphonuclear leukocytes sometimes appeared in the scrapings.

## TREATMENT

The impossibility of making an unequivocal clinical diagnosis of epidemic keratoconjunctivitis before corneal opacities develop complicates the evaluation of methods of treatment, since rapid recovery and the prevention of corneal opacities constitute the criteria of effective treatment. Fortunately, however, Sanders [16] provided a means of verifying the diagnosis when he showed that a patient recovering from the disease possessed a substance in the blood serum which when mixed with dilutions of his virus prevented death in mice. This virus-neutralizing substance could be expressed by the reverse of the dilution factor. If the patient's serum-virus mixture diluted to titers of $10^{-2}$, $10^{-3}$, $10^{-4}$, $10^{-5}$ and $10^{-6}$ killed mice in dilutions of $10^{-2}$ and $10^{-3}$ but failed to produce symptoms in higher dilutions, and if the normal serum-virus mixture diluted similarly killed all mice through dilutions up to and including $10^{-6}$, the patient's serum had 10,000 units of neutralizing substance. Sanders [16] observed that patients with other types of conjunctivitis, including Béal's, did not have this substance in their serum.

A total of 296 patients with epidemic keratoconjunctivitis were treated. Of these, 209 had symptomatic treatment. In all but 2 patients corneal opacities developed. In these 2 patients there was considerable doubt as to the accuracy of the original diagnosis, and, unfortunately, neither of them has been available for check-up of the antibody titer. Since the diagnosis for both patients was made during the height of the epidemic, however, their condition was classified as epidemic keratoconjunctivitis in spite of the questionable diagnosis.

*Sulfonamide Compounds.*—Thirty-five patients were treated with sulfathiazole, 25 patients with an ointment containing 5 per cent sulfathiazole in anhydrous wool fat and petrolatum and 10 patients with 3 per cent solution of sodium sulfathiazole sesquihydrate. Clinically none of these patients was benefited by the therapy, and many of them complained that the local use of sulfathiazole ointment increased their symptoms. In an effort to evaluate therapy with the sulfonamide compounds experimentally, 48 white mice were fed sulfathiazole by mouth for two days and then given injections of various dilutions of the virus (table 3), 8 mice being used for each dilution. Five-tenths gram of sulfathiazole and 1.5 Gm. of sodium bicarbonate were mixed with 100 Gm. of a casein food, and each mouse received 5 Gm. of the mixture a day. This is a standard method of protecting mice against streptococcic and pneumococcic infections. There was no evidence of protection against the virus, however, and treatment of 48 mice with sulfadiazine in a similar manner (table 4) yielded equally negative results. Clinically and experimentally sulfathiazole and sulfadiazine were observed to have no effect on the virus.

*Penicillin.*—Local application of an ointment containing penicillin (500 units per gram of an oxycholesterol-petrolatum base) was used with 3 patients, with no effect. Huang [18] reported

17. Bedell, A. J.: Epidemic Keratoconjunctivitis, New York State J. Med., to be published.

18. Huang: Personal communication to the author.

to me that in his experience penicillin has had no effect on the virus when tested in vitro.

*Tyrothricin.*—This drug was used for 10 patients in solutions of 48 and 20 mg. per hundred cubic centimeters. Nearly all patients experienced some symptomatic improvement, but to about the same extent as that reported by patients using tetracaine and epinephrine. The duration of the acute phase of the disease seemed to be shortened, but in all 10 patients a large factors are involved, however, since deaths in mice occurred erratically. One must conclude that experimentally tyrothricin had little or no effect on the virus and that clinically, although the severity of the acute conjunctivitis was decreased, the disease ran a normal course; this was true even though 2 of the patients were given tyrothricin on the first day of the disease.

*Convalescent Plasma.*—The presence of antibodies noted by Sanders suggested the thera-

TABLE 3.—*Results of Feeding Sulfathiazole to Mice Inoculated with Virus of Epidemic Keratoconjunctivitis*

| Date | Dilution of Virus $10^{-1}$ | $10^{-2}$ | $10^{-3}$ | $10^{-4}$ | $10^{-5}$ | $10^{-6}$ |
|---|---|---|---|---|---|---|
| 5/17 Mice fed mixture * | | | | | | |
| 5/19 Injection | | | | | | |
| 5/20 | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| 5/22 | D D D — | — — — — | — — — — | — — — — | — — — — | — — — — |
| | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| 5/23 | D | D D D D | D D D D | D D D D | — — — — | — — — — |
| | D D D D | D D D D | D D D D | D D D — | — — — — | — — — — |
| 5/24 | ..... | ..... | ..... | D | D D D — | D — — — |
| | | | ..... | ..... | — — — — | — — — — |
| 5/25 | ..... | ..... | ..... | ..... | D | — — — |
| | | | ..... | ..... | D — — — | — — — — |
| 5/26 | ..... | ..... | ..... | ..... | ..... | — — — |
| | | | ..... | ..... | D D — | — — — — |
| 5/27 | ..... | ..... | ..... | ..... | ..... | — — — |
| | | | ..... | ..... | D | — — — — |

* Each mouse data on which appear in this table and in table 4 was fed 5 Gm. of a mixture containing 0.5 Gm. of sulfathiazole sodium and 1.5 Gm. of sodium bicarbonate per hundred grams of casein food.

TABLE 4.—*Results of Feeding Sulfadiazine to Mice Inoculated with Virus of Epidemic Keratoconjunctivitis*

| Date | Dilution of Virus $10^{-1}$ | $10^{-2}$ | $10^{-3}$ | $10^{-4}$ | $10^{-5}$ | $10^{-6}$ |
|---|---|---|---|---|---|---|
| 5/17 Mice fed mixture | | | | | | |
| 5/19 Injection | | | | | | |
| 5/20 | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| 5/22 | D D — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| | — — — — | — — — — | — — — — | — — — — | — — — — | — — — — |
| 5/23 | D D | D D D D | D D D D | D D D — | — — — — | — — — — |
| | D D D D | D D D D | D D — — | — — — — | — — — — | — — — — |
| 5/24 | ..... | ..... | ..... | D | D D — — | — — — — |
| | | | D D | D D D D | — — — — | — — — — |
| 5/25 | ..... | ..... | ..... | ..... | D D | — — — — |
| | | | ..... | ..... | — — — — | — — — — |
| 5/26 | ..... | ..... | ..... | ..... | ..... | D — — — |
| | | | ..... | ..... | D D — — | — — — — |
| 5/27 | ..... | ..... | ..... | ..... | ..... | D — — |
| | | | ..... | ..... | D D | — — — — |

number of corneal opacities developed. Several in vitro tests were attempted. The results were difficult to evaluate, since the tyrothricin-virus mixtures when allowed to stand at room temperature did not kill mice in higher dilutions. After the mixture had stood two hours at room temperature few deaths occurred with dilutions of $10^{-5}$ and $10^{-6}$. A comparison of these results with those for the control series indicates that there is deterioration of the virus when it is allowed to stand at room temperature. Other

peutic use of convalescent serum or plasma.[19] In order to test the effect of convalescent plasma on formation of antibodies, 5 patients with other types of conjunctivitis were given 50 cc. and 1 patient was given 100 cc. of the serum intravenously (table 5). Samples of blood taken from these patients at intervals up to three months were tested for the presence of antibodies.

19. Braley, A. E., and Sanders, M.: Treatment of Epidemic Keratoconjunctivitis: Preliminary Report of Ten Cases, J. A. M. A. **121**:999-1000 (March 27) 1943.

Only 1, the patient who had received 100 cc. of plasma, presented any evidence of a neutralizing substance. She was a physician, with severe pneumococcic conjunctivitis involving her only eye, and she was given this amount of plasma because she had not responded rapidly to local sulfonamide therapy. She has not been available for a final check on the antibody titer of her serum, but it was very low at the end of two months. The conclusion drawn from these tests was that convalescent plasma given in amounts of 50 cc. was insufficient to affect the test for antibodies.

TABLE 5.—*Results of Intravenous Administration of Plasma of Patients Convalescing from Epidemic Keratoconjunctivitis to Patients with Other Types of Conjunctivitis*

| Case | Diagnosis | Amount of Convalescent Plasma, Cc. | Resultant Titer of Serum |
|---|---|---|---|
| 1 | Staphylococcic conjunctivitis | 50 | — |
| 2 | Pneumococcic conjunctivitis | 100 | 10 — (?) |
| 3 | Burns of skin | 50 | — |
| 4 | Acute conjunctivitis of unknown origin | 50 | — |
| 5 | Erythema multiforme | 50 | — |
| 6 | Chronic staphylococcic keratoconjunctivitis | 50 | — |

TABLE 6—*Results of Convalescent Plasma Therapy*

| Case | Name | No. of Days of Disease Before Administration of Convalescent Plasma | Amount of Convalescent Plasma, Cc. | Results of Corneal Change | Final Titer of Patient's Serum |
|---|---|---|---|---|---|
| 1 | G. T. | 8 | 50 | 1+ | 10,000 |
| 2 | M. T. | 3 | 40 | — | 10,000 |
| 3 | B. T. | 2 | 20 | — | 10,000 |
| 4 | M. N. | 5 | 40 | — | 10,000 |
| 5 | A. S. | 6 | 30 | 1+ | 10,000 |
| 6 | J. S. | 6 | 40 | 3+ | 10,000 |
| 7 | D. S. | 4 | 15 | 1+ | 1,000 |
| 8 | J. L. | 6 | 25 | — | 10,000 |
| 9 | H. T. | 5 | 50 | — | 1,000 |
| 10 | M. F. | 4 | 40 | — | 1,000 |
| 11 | E. L. | 5 | 50 | — | 1,000 |
| 12 | W. K. | 1 | 50 | — | 1,000 |
| 13 | B. M. | 2 | 50 | — | 1,000 |
| 14 | L. M. | 9 | 50 | 4+ | 10,000 |
| 15 | H. H. | 1 | 50 | — | 1,000 |
| 16 | B. S. | 3 | 50 | — | 1,000 |
| 17 | W. M. | 4 | 50 | 1+ | 1,000 |
| 18 | E. Y. | 1 | 50 | — | 1,000 |
| 19 | H. S. | 7 and 9 | 100 | 4+ | 100 |
| 20 | A. H. | 4 | 50 | — | 1,000 |
| 21 | M. G. | 2 | 50 | — | 1,000 |
| 22 | M. P. | 2 | 50 | — | 10,000 |
| 23 | M. L. | 3 | 50 | — | 1,000 |
| 24 | L. P. | 9 | 50 | 4+ | 10,000 |
| 25 | J. F. | 5 | 50 | — | 1,000 |
| 26 | M. G. | 4 | 50 | — | 100 |
| 27 | W. G. | 2 | 50 | — | 1,000 |
| 28 | H. C. | 3 | 50 | — | 100 |
| 29 | S. S. | 5 | 50 | 3+ | 1,000 |
| 30 | H. B. | 5 | 50 | 1+ | 1,000 |
| 31 | W. S. | 7 and 9 | 100 | 4+ | 10,000 |
| 32 | L. N. | 4 | 50 | — | 1,000 |
| 33 | W. L. | 3 | 50 | — | 1,000 |
| 34 | W. F. | 9 | 50 | 4+ | 100 |
| 35 | W. T. | 3 | 50 | — | 1,000 |
| 36 | P. P. | 2 | 50 | — | 1,000 |
| 37 | T. G. | 3 | 50 | — | 100 |
| 38 | S. S. | 4 | 50 | — | 1,000 |
| 39 | L. S. | 5 | 50 | — | 1,000 |
| 40 | D. D. | 4 | 50 | — | 100 |
| 41 | B. B. | 3 | 50 | — | Sample lost |
| 42 | P. H. | 2 | 15 | — | 100 |
| 43 | F. H. | 2 | 20 | — | 1,000 |
| 44 | K. M. | 3 | 30 | — | 100 |
| 45 | M. K. | 4 | 20 | — | 100 |
| 46 | P. G. | 3 | 15 | — | 100 |
| 47 | G. W. | 6 | 20 | 1+ | 100 |

Convalescent plasma was administered to 47 patients for whom a diagnosis of epidemic keratoconjunctivitis had been made. Samples of serum were obtained from these patients at intervals (table 6). None of the serum which was obtained during the acute disease had virus-neutralizing antibodies. The neutralizing substances became apparent in from one to three months. Patient 19 is of particular interest because she did not show any response to the plasma, and the development of antibodies was slow. In spite of the presence of many corneal opacities, there was no evidence of antibodies until three months after the opacities developed.

When the results of this experiment are expressed in a graph, it is evident that little, or no, effect was obtained when the plasma was given after the seventh or eighth day (fig. 4); good results were obtained when the plasma was given before the fifth day, and inconsistent results, some good and some poor, when the plasma was given after the fifth day. Whereas corneal opacities developed in 99 per cent of all patients not treated with convalescent plasma, they developed in only 30 per cent of patients treated with convalescent plasma. Corneal opacities developed in the majority of patients treated after the fifth day. This failure of the convalescent plasma to effect cure after the disease was established is consistent with results obtained in the treatment of other virus diseases for which convalescent plasma or serum has been of value during the incubation period or the first days of the illness.[20]

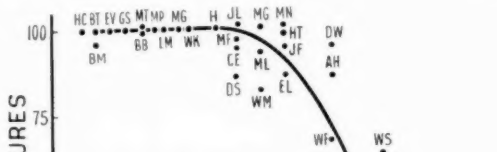


Fig. 4.—Results of administration of convalescent plasma to 36 patients with epidemic keratoconjunctivitis.

20. Van Rooyen, C. E., and Rhodes, A. J.: Virus Diseases of Man, New York, Oxford University Press, 1940.

A control series of 5 patients with epidemic keratoconjunctivitis were given 50 cc. of normal plasma intravenously (table 7). The normal plasma had no effect on the progress of the disease or on the development of antibodies in the serum.

TABLE 7.—*Results of Injection of Normal Plasma on Patients with Epidemic Keratoconjunctivitis*

| Case | Day of Disease Injection Was Given | Amount of Normal Plasma, Cc. | Resultant Corneal Changes | Final Serum Titer |
|---|---|---|---|---|
| 1 | 4 | 50 | 4— | 1,000 |
| 2 | 6 | 50 | 4— | 10,000 |
| 3 | 3 | 50 | 4— | 1,000 |
| 4 | 5 | 50 | 4— | 1,000 |
| 5 | 2 | 50 | 4— | 100 |

## COMMENT

Epidemic keratoconjunctivitis, while new to this continent, has occurred in epidemics elsewhere in the world. In these epidemics observers have emphasized the presence of corneal opacities. As in trachoma, in which pannus must be present before the diagnosis can be made, the subepithelial infiltration of the cornea characteristic of epidemic keratoconjunctivitis must be present before an unequivocal clinical diagnosis is possible. The diagnosis can also be made on the basis of the development of virus antibodies, but as antibody titer can be detected only long after the disease has run its course, this method is of no value in making an early diagnosis. In the acute phase of the disease, then, the diagnosis is presumptive and must remain so until corneal opacities develop or virus-neutralizing substances can be measured.

## SUMMARY AND CONCLUSIONS

Epidemics of a disease similar to epidemic keratoconjunctivitis have been reported at intervals since 1889.

The current epidemic probably began in Malaya, in 1938, from whence it spread to Hawaii and to the continental United States.

The epidemiology is obscure, but clinics, dispensaries and physicians' offices must be considered sources of transmission. Scrupulous care should be given to the cleansing of hands and instruments, and the use of individual droppers is recommended.

The clinical disease may be divided into three stages: (*a*) abrupt onset of edema, associated with a foreign body sensation; (*b*) follicular conjunctivitis and pseudomembrane formation, with lymphadenopathy and symptoms of involvement of the upper respiratory tract, and (*c*) retrogression of the conjunctivitis with development of corneal opacities.

The etiologic agent is probably a filtrable virus, the observations in the present study substantiating those of Sanders.

Patients recovering from the disease have immune bodies for the virus in their serums.

The sulfonamide compounds and penicillin have no effect on the virus.

Tyrothricin probably has no effect on the virus.

Convalescent plasma or serum, administered before the fifth day of the disease, is the treatment of choice.

Corneal opacities developed in 99 per cent of the patients treated symptomatically but in only 30 per cent of patients treated with convalescent plasma.

# BRUCELLOSIS

LIEUTENANT COMMANDER HAROLD J. HARRIS (MC), U.S.N.R.

Brucellosis is an infectious disease of manifold symptoms. The eye is one of the many sites of its manifestations, although the disease is relatively rarely recognized through its ocular signs. In its acute or its chronic form, brucellosis is second to no other disease, syphilis not excluded, in its ability to masquerade under innumerable guises.

Of the pathology, only enough will be said to show why the symptoms may be so varied. The organism has been isolated from the heart in cases of endocarditis and pericarditis; from the lung in cases of pleurisy and pneumonia; from the liver in cases of necrosis and abscess; from the gastrointestinal tract in cases of ulceration of the small and large bowel and of appendical infection; from the mesenteric lymph nodes; from the spleen in cases of necrosis; from the fallopian tubes in cases of salpingitis; from the ovary in cases of infected cyst; from the gallbladder in cases of acute and chronic cholecystitis; from the pancreas in cases of abscess; from the kidney in cases of pyelonephritis; from the bone in cases of osteomyelitis; from abscess of the mediastinum; from the joints in cases of acute and chronic suppurative and nonsuppurative arthritis and hydrarthrosis; from the testes, epididymis and prostate; from the skin in cases of chronic subcutaneous abscess and ulceration; from the mammary gland in cases of mastitis; from the tonsils; from the lymph nodes in virtually all regions of the body; from the central nervous system in cases of meningitis, encephalitis and myelitis; from the placenta, and from the human fetus. From all these tissues, as well as from the blood, spinal fluid, urine and stool, the organism has been cultured by one or more investigators.

There is no characteristic histopathologic picture. Proliferation of the cells of the reticuloendothelial system and infectious granuloma resembling the tubercle were pointed out by Sharp.[1] Confusion with tuberculosis was warned against by Amoss, by Fleischner and Meyer and by others.

Read at a meeting of the New York Society for Clinical Ophthalmology, May 1, 1944.

1. Sharp, W. B.: Pathology of Undulant Fever, Arch. Path. **18**:72-108 (July) 1934.

## OCULAR MANIFESTATIONS

Green,[2] of St. Louis, published one of the earliest reports concerned exclusively with ocular manifestations in brucellosis. He stated that the occurrence of such signs in the course of brucellosis was well established but that comparatively few ophthalmologists had taken advantage of the opportunity to determine by laboratory methods the presence or absence of past or present infection with brucella organisms. He reported 4 of his own cases and cited 28 others from the literature, in 11 of which culture of the blood or the spinal fluid yielded the organisms. Green's own series included 1 case of recurrent phlyctenular conjunctivitis and corneal ulcer, 1 of retinal hemorrhage, 1 of optic neuritis and 1 of retinochoroiditis, clinically attributable to brucellosis. The cases reviewed included 1 or more each of the following conditions: iritis; optic neuritis (with or without atrophy); panophthalmitis; iridochoroiditis; septic retinitis; papilledema; hemorrhagic retinitis; palsies of ocular muscles; iridocyclitis, and keratitis, associated with or independent of brucella meningitis or meningoencephalitis.

Green pointed out that most ocular lesions occurring in the course of brucellosis do not destroy the integrity of the globe and that enucleation is therefore not demanded. This explains the lack of studies on the pathologic changes in the human eye. He called attention to Orloff's study of eyes of guinea pigs which had died. Orloff had stressed the practical importance of the ocular infections associated with brucellosis, commenting that they seemed to have great similarity, clinically as well as pathologically, to ocular tuberculosis.

Rutherford[3] stated:

> Melitensis infection of the central nervous system occurs occasionally with or without ocular complications. [In 3 of 63 cases of undulant fever] there were bilateral papilledema, an increase in the spinal fluid pressure, mononuclear pleocytosis and evidence on which to base a diagnosis of infection of the central

2. Green, J.: Ocular Manifestations in Brucellosis, Arch. Ophth. **21**:51-65 (Jan.) 1939.

3. Rutherford, C. W.: Papilledema in Undulant Fever: Report of Cases, J. A. M. A. **104**:1490-1492 (April 27) 1935.

nervous system by some variety of the melitensis organism. . . .

. . . Papilledema is occasionally found in patients in whom the symptomatology is indefinite and leading signs are absent. It is in such cases that undulant fever should be considered in the differential diagnosis.

Carpenter and Boak [4] also noted the lesions of the eye produced by brucella infection and stated that they were similar to those produced by infection with the tubercle bacillus. That many cases of Brucella involvement of the eye have been ascribed to tuberculosis can scarcely be doubted.

Braley [5] saw several cases of choroiditis associated with chronic brucellosis but was never able to isolate the organism. He noted that the eyes healed rapidly with vaccine therapy and that they also healed with no treatment but healing required more time. In various cases he ascribed acute iritis, acute choroiditis and chronic iritis, iridocyclitis and choroiditis to brucellosis.

There seems good reason to bear in mind Green's comment [2]:

An immense amount of work has been done on brucellosis in the past twenty years. Those who have undertaken the study of the disease either in the laboratory or clinically have become enthusiastic about the possibilities and implications of this new malady; in fact, one is inclined to feel that some authors have allowed their enthusiasm to outrun their judgment. Evidence is accumulating, however, that some ocular maladies ascribed to other origins may be caused by brucellosis. The external ocular muscles, the cornea, the uveal tract, the retina and the optic nerve have all proved vulnerable. Who has not been thwarted in his most painstaking efforts to establish the cause of a chronic uveitis? Should not the ophthalmologist include in his list of possible etiologic factors a disease that is widespread and one which has been proved to be capable of affecting almost every tissue of the body?

Although I have been thought to be one of those who are overenthusiastic about the possibilities and implications of this infection, I have reported few instances of ocular involvement.[6] This was due not to the paucity of cases with ocular manifestations but to my almost complete lack of knowledge concerning the eye, which prevented evaluation of the cases encountered. The ophthalmologists to whom these patients were referred treated them empirically, also without suspecting the origin of their infection. Fortunately, there were few serious eventualities, either because there was spontaneous remission or because these patients also were treated with brucella vaccine.

The greatest handicap in the proper evaluation of ocular involvement—or indeed in any manifestation of brucellosis—is the difficulty in obtaining accurate cultural studies. This is due not only to the lack of interest on the part of most bacteriologists, and laboratory technicians, and, I am sorry to say, of physicians also, in this so-called rare disease, but to the technical difficulties in growing the organism, especially the Brucella abortus strain.[7]

One of the first patients in whom I noted ocular manifestations was a school teacher aged 35 who was referred to me by Dr. Ralph Greene.[8] She had had repeated exacerbations of brucellosis for several years, with diplopia and a recurrent cervicosympathetic syndrome with each attack.

Probably my first recognition of iritis [9] as a part of the clinical manifestation of brucellosis occurred in May 1941, not long after the beginning of my Naval service.

A sailor aged 24 was sent to me for an opinion as to whether he was malingering, psychoneurotic or really sick. He complained of headache, joint and muscle pains, epigastric distress, pronounced fatigue and productive cough. No cause for his complaints had been found during three months of careful study except for moderate secondary anemia and recurrent severe iritis. The results of all studies were without significance until the tests for brucellosis were made. The iritis had recurred four or five times a year, together with low grade fever, over a period of five years. Each summer for eight years there had been attacks of chills and fever of unknown origin, the period of the attacks lasting from three to five weeks. An agglutination test of the blood for brucellosis gave a negative reaction (as is usually true with chronic brucellosis); the cutaneous reaction was positive, and the phagocytic index was low. The patient was transferred to my wards for further observation. Br. abortus vaccine was given, with only temporary improvement in the subjective symptoms and in the recurrent attacks of iritis. The iritis at first recurred in spite of vaccine therapy, until use of the vaccine intravenously was followed by a high phagocytic response and freedom from the attacks for several months. I was detached from the hospital shortly after the attack on Pearl Harbor and so was prevented from ordering a trial of artificial fever therapy for him. About a month later, because of his failure to recover completely from his illness, which had existed long before his enlistment, he was discharged from the service. Three months after I had last seen him his family reported that he had had another attack of iritis, that there had

4. Carpenter, C. M., and Boak, R. A.: Undulant Fever: Sources, Modes of Infection and Prophylaxis, Am. J. M. Sc. **185**:97-109, 1933.

5. Braley, A.: Personal communication to the author, April 1944.

6. Harris, H. J.: Brucellosis (Undulant Fever): Clinical and Subclinical, New York, Paul B. Hoeber, Inc., 1941.

7. Poston, M. A.: Studies in Chronic Brucellosis: III. Methods Used in Obtaining Cultures, Pub. Health Rep. **53**:1-4, 1938.

8. Greene, R.: Personal communication to the author, May 1941.

9. Harris, H. J.: Chronic Brucellosis with Recurrent Iritis, Hemiplegia and Death from a Complicating Diffuse Encephalitic Encephalomalacia, U. S. Nav. M. Bull. **41**:517-520, 1943.

been several attacks of vertigo, during one of which vision was much reduced and that twice he had stumbled and fallen, for no apparent reason, while going upstairs. For ten days he had complained of severe headaches, usually lasting only a few minutes and generally accompanied by stiffness of the neck. Soon thereafter sharp pain had developed in the left frontal region, and about four days later his right leg became weak, with a tendency to limp. He had noted difficulty in concentrating. On March 20, 1942 he had sudden right hemiplegia and was admitted to the University of Kansas Hospital, to the service of Dr. Frank Teachenor. His right pupil was slightly larger than the left; both pupils reacted to light, and there was a questionable degree of choking of the left optic disk. The spinal fluid examined on April 3, 1942, was under 260 mm. of pressure and was clear, with 33 white cells (85 per cent lymphocytes) per cubic millimeter and 119 mg. of total protein per hundred cubic centimeters. On April 9 a ventricular cannula passed toward the left lateral ventricle through a burr hole just to the left of the midline met with lack of the usual resistance. A biopsy cannula, passed into the same region of the frontal lobe, brought forth soft, reddish brown, granular tissue. Operation was discontinued, but the patient died the same day. Histologic examination, by Dr. H. R. Wahl, showed extensive acute and chronic inflammatory reaction in the pons and in the region of the left internal capsule, with a well marked, cufflike accumulation of monocytes and polymorphonuclear leukocytes in the perivascular spaces. Dr. Wahl stated that death was due to "a rather severe acute and chronic form of encephalitis," which conformed to the type reported by Sharp,[1] De Jong[10] and others as of brucella origin.

Dr. William Rose referred a woman aged 26 to me on June 13, 1942 for performance of the multiple tests for brucellosis because of the suspicion that her attacks of keratitis and conjunctivitis might be due to this condition. The attacks had been recurrent for about four years and were confined to the right eye. They were accompanied with severe pain, headaches, tearing and progressive loss of vision, clearing up for varying periods except for residual blurred vision. Use of the eyes seemed to precipitate attacks. Herpetic keratitis, vitamin deficiency, allergy, anemia and syphilis had been suggested and ruled out as etiologic factors. In addition to the ocular manifestations, the patient had complained of weakness, mental confusion, joint and muscle pains, headache and vague gastrointestinal symptoms. She was afebrile, but there was a history of recurrent chills and fever three or four years previously. She had drunk raw milk for many years. On June 13 the agglutination reaction was negative for brucellosis, the cutaneous reaction positive and the phagocytic index low (phagocytosis was pronounced in 2 cells, moderate in 8 cells, slight in 12 cells and absent in 3 cells; index, 2-8-12-3). The presence of the positive cutaneous reaction was interpreted as evidence of a past or still existing brucella infection. The low phagocytic index in the presence of the positive cutaneous reaction and systemic symptoms referable to brucellosis was interpreted as presumptive evidence of brucellosis from which the patient had not recovered. Br. abortus vaccine was administered as a therapeutic test by Dr. Rose, and there was steady improvement both in constitutional manifestations and in the ocular condition coincident with a pronounced rise in the phagocytic index. On July 27 the opsonocytophagic index was 16-9-0-0 and on August 22 it was 20-5-0-0. On this date the patient reported that she felt entirely well and showed great improvement in the condition of the eyes. Within four months there was complete clinical recovery, and the phagocytic index still showed a high degree of resistance (18-7-0-0). There has not been any recurrence of keratitis for more than eighteen months, and the patient has been working steadily for over a year. There was a recent mild recurrence of constitutional symptoms, accompanied, as is so frequently significant, by a fall in the phagocytic index to 5-7-6-7. Soon after vaccine treatment was again instituted, these symptoms disappeared coincidentally with a satisfactory rise in the phagocytic power of the white cells. There were no ocular manifestations.

Brucella vaccine treatment cannot be relegated to the category of nonspecific shock therapy. In the majority of patients reactions to vaccine are best avoided entirely. The clinical improvement almost invariably parallels the rise in the phagocytic power of the white cells, and relapse all too often occurs if the phagocytic index is not kept at a high level until there has been a long period of clinical recovery. The response that has so often been reported to follow intravenous administration of typhoid vaccine may be the result of nonspecific shock therapy, or it may produce whatever doubtful results are obtained through production of fever. No one has shown that such nonspecific therapy produces more than transient improvement. In patients treated with this method early in my work[11] with brucellosis, in 1932 and 1933, relapse occurred so soon and so consistently that the method was abandoned. The good results reported by many authors were, I believe, published too early and represented too small a number of cases to be considered significant.

Two brothers were recently referred to me for an opinion by Dr. A. C. Krause, chief of the department of ophthalmology of the University of Chicago. One of them, aged 37, had a history of recurrent uveitis since April 1943, preceded by a history of chronic arthritis since 1937. The other patient, aged 44, had a history of iritis, keratitis, conjunctivitis and episcleritis, involving first the right and later the left eye, which had been recurrent since 1938. In 1940 his tuberculin reaction had been moderately positive, and the intradermal test with brucella antigen had given strongly positive results. The agglutination reaction had been negative for brucellosis. Ten days after the cutaneous test for brucellosis a small paracentral scotoma on the right of the fixation point was noted in the left eye. Two weeks later, thirty-six hours after injection of 0.1 cc. of a mixed filtrate of brucellas, a central scotoma appeared, and a small reddened area of hemorrhage was noted just above the fovea. The diagnosis was acute chorioretinitis, with macular edema, hemorrhage and absence of the macular reflex, in the left eye. A month later two globular hemor-

10. De Jong, R. N.: Central Nervous System Involvement in Undulant Fever with the Report of a Case and a Survey of the Literature, J. Nerv. & Ment. Dis. **83**:430-442, 1936.

11. Harris, H. J.: Undulant Fever (Brucellosis): Difficulties in Diagnosis and Treatment, New York State J. Med. **37**:1295-1301, 1937.

rhages, nasal to the macula, were noted. In March 1942, after regression of this process, new small hemorrhages appeared nasal to the macular region of the left eye. Careful study for evidence of perivascular disease, including biopsy of muscle tissue, gave negative results. Further hemorrhages were noted in April, June and July 1942. In October 1942 the patient exhibited a central scotoma 10 degrees in diameter in the left eye. At that time he complained of severe fatigue. A diagnosis of chronic brucellosis and central retinitis, probably due to brucellosis, was made by Dr. Krause. Other laboratory studies showed a relatively low white blood cell count, ranging from 3,800 to 5,900, with a normal differential count. In March 1942 the sedimentation rate was 20 mm. in one hour. Agglutination tests with Br. abortus prior to the cutaneous test gave negative results. The Wassermann and Kahn reactions of the blood were normal. Urine and all other routine and special studies revealed nothing abnormal.

The patient furnished additional data concerning himself, including the history of low grade fever and extreme fatigue (to the degree that he spent the winter of 1940-1941 in bed), arthritic pains and recurrent diarrhea, occurring between visits to the ophthalmic clinic. Bizarre results of urinalysis were reported. On Sept. 17, 1943 there were a 2 plus reaction for albumin and a 3 plus reaction for sugar, hyaline casts and 2 to 3 pus cells per high power field. On December 28 there was no albumin and no casts, and the reaction for sugar was 2 plus. On Jan. 26, 1944 examination showed a faint trace of albumin, no sugar and occasional hyaline and granular casts, with similar results on February 16. On May 14, 1943 the laboratory of the Illinois state department of public health had reported isolation of brucella organisms from a specimen of stool.

This patient's experience with a commercial mixed vaccine and with a mixed filtrate emphasizes one of the few dangers from vaccine therapy. Both the preparations may be productive of severe local, focal and systemic manifestations. With ophthalmic complications, as well as infections of the central nervous system, reactions are to be assiduously avoided. This can be accomplished by use of the plain Br. abortus vaccine, diluted to any necessary degree.

Abnormal constituents of the urine, such as are described in this case, are not rare in cases of brucellosis. Nephritis, as evidenced by albuminuria and the presence of hyaline and granular casts, has been encountered repeatedly in the course of brucellosis. To the coincident or unrelated appearance of glycosuria, with or without hyperglycemia, I [6] have previously called attention.

## DIAGNOSIS

In order to obtain an accurate diagnosis one must (1) disabuse one's mind of the almost universally prevalent idea that the agglutination test is the one and infallible diagnostic procedure and (2) evaluate properly the multiple tests that are available.

The agglutination test of the blood is negative in the majority of cases of chronic infection with the brucella.[12] The positive reaction then is frequently in low dilutions only. This test, therefore, is valuable alone only when it gives positive results in dilutions of 1:80 or higher. A positive reaction in low dilution is suggestive of brucella infection, but may rarely occur as a cross agglutination in the presence of infection with Pasteurella tularensis, Eberthella typhosa or Bacillus proteus X 19. A negative reaction to the agglutination test does not rule out brucellosis. If that one point were sufficiently understood, fewer brucella infections would remain undiagnosed.

The intradermal test also has its limitations and points about which there is still confusion. Perhaps it is simplest to say that in all respects this test is comparable to the tuberculin test. A positive reaction indicates only that at some time the patient has been infected. It gives no information as to the present status of the infection. It is only in the presence of a moderate or low degree of phagocytic power of the white cells, plus clinical symptoms referable to brucellosis, that the cutaneous test becomes a valuable aid in diagnosis.

It is essential that the test not be ignored if the reaction is only weakly positive. A weakly positive reaction has the same significance as a strongly positive one, except that it indicates a lesser degree of sensitivity to brucella protein. This is a valuable guide to the proper dilution of vaccine to be used if vaccine therapy is indicated.

The test is preferably made with 0.1 cc. of a heat-killed vaccine prepared from the abortus strain only, in a concentration of 2,000,000,000 organisms per cubic centimeter. The mixed vaccines are likely to produce unnecessarily severe reactions. Brucellergin,[13] a filtrate of the three strains, is apparently much less sensitive as an antigen.[14] The reaction should be read at the end of four days. If the result is then negative or equivocal, it should be read again at the end of seven or eight days because of the possibility of delayed reaction.

Like the agglutination test, the cutaneous test may give a negative reaction even in the presence of a positive culture.[12] However, if a sensitive

12. Evans, A. E.; Robinson, F. H., and Baumgartner, L.: Studies on Chronic Brucellosis: IV. Evaluation of the Diagnostic Laboratory Tests, Pub. Health Rep. **53**:1507-1525, 1938. Harris.[6]

13. Huddleson, I. F.: Brucellosis in Man and Animals, New York, Commonwealth Fund, 1943.

14. Angle, F. E.; Algie, W. H.; Baumgartner, L., and Lunsford, W. F.: Skin Testing for Brucellosis (Undulant Fever) in School Children, Ann. Int. Med. **12**:1189-1193, 1939.

antigen is used, such a result will occur in probably only about 5 per cent of cases.

The opsonocytophagic test is performed for two purposes: (1) to determine the degree of specific resistance of the patient as an aid in interpreting the significance of the cutaneous reaction, and (2) to provide a base line for comparison with future tests if the patient is to have vaccine therapy. The test if performed alone has little significance.

The test must be done with the most careful technic. The specimen of blood must be fresh—not more than three hours old. A viable stock culture of the brucella must be regrown by transplantation on a fresh liver-agar or bactotryptose-agar slant and incubation for forty-eight hours before it is to be used for the test. Nonvirulent cultures will give falsely high readings. The blood film, made after the suspension of live brucella organisms has been mixed with the patient's blood and incubated, must be carefully prepared and well stained with Wright's or Hasting's stain. The actual number of bacteria ingested by each of twenty-five polymorphonuclear leukocytes must be counted. The number of cells showing pronounced, moderate, slight and no phagocytic activity gives the direct measure of the patient's resistance to brucella infection.

As already stated, patients under treatment with Br. abortus vaccine will show a progressive increase in the phagocytic power of the white cells which is virtually always commensurate with their clinical improvement. By means of regularly repeated determinations of the phagocytic index after cessation of treatment the patient's status may be accurately checked. Relapse may usually be predicted in the presence of a falling index in patients who are not actually free of infection.

The presence of the organisms on culture of blood, pus, urine, bile, prostatic fluid, stool, or other fluid or tissue furnishes the only definitive laboratory test. In cases of chronic infection culture is exceedingly unrewarding, especially infections with Br. abortus.[7] Culture should be undertaken whenever possible, however, and with the most careful technic, 5 to 10 per cent of carbon dioxide in air and special mediums being used and prolonged observation made. Animal inoculation is essential to accurate results. The guinea pigs must be kept nearly sixteen weeks in some instances. Poston was able to recover the organism from the blood of 5 of 14 chronically ill patients for whom all tests, including culture by the usual methods, had given negative results. Brucella melitensis and Brucella suis are more readily recovered, particularly the melitensis strain, in the presence of the febrile illness. The great need is for laboratories in which there are facilities for and personnel interested in these procedures. In addition to its furnishing positive proof of diagnosis, a positive culture may be of inestimable value in pointing to the localization of infection, and therefore to measures for its eradication.

### TREATMENT

In cases of the acute illness the most valuable aid is sulfadiazine or sulfathiazole, although neither substance may be said to be actually curative. Remission is likely to occur, at which time vaccine may be employed for the purpose of building up adequate resistance. Transfusions of immune or nonimmune blood may be successful, as may Foshay's antiserum, in bringing about remission. To bring about actual cure is the problem. Artificial fever therapy is, I am afraid, overrated in some quarters, for either the acute or the chronic illness. It is successful probably in only a small percentage of cases.[15] Much of the probable error in its evaluation has been made on the basis of too hasty a decision as to recovery and of inadequate follow-up study. However, its trial is justified in selected cases, especially those in which the disease is refractory to vaccine therapy.

In intestinal localization of infection, succinylsulfathiazole or sulfaguanidine may prove to be of greatest value, especially in prevention of relapse.

In treatment of the chronic illness vaccine made from the abortus strain alone has proved to be of greatest value in my experience. Satisfactory results in approximately 75 per cent of more than 400 patients treated by this method have been achieved, with good results in 15 or 20 per cent and failures in 5 to 10 per cent. When vaccine fails to bring about recovery through intramuscular use, it is usually tried intravenously. By this route rather sharp reactions are usually produced, whereas reactions are deliberately avoided with the intramuscular administration. Use of O'Neil and Foshay's[16] nitrous acid–treated vaccine is also a valuable

15. Harris, H. J.: Physical Therapy of Various Manifestations of Brucellosis (Undulant Fever), Arch. Phys. Therapy **21**:605-611, 1940; Brucellosis, Bull. New York Acad. Med. **19**:631-655, 1943. Simpson, W. M.: Brucellosis (Undulant Fever), in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1940, vol. 4, chap. 24, pp. 99-108. Harris.[6]

16. O'Neil, A. E.: Preliminary Note on the Treatment of Undulant Fever in Man with Detoxified Vaccine and with Antiserum, Ohio State M. J. **29**:438-439, 1933. Foshay, L.: Personal communication to the author, September 1939.

method in management of the chronic or the subacute illness.

The sulfonamide compounds are usually of little value for the chronic illness except in cases of localized infections. Succinylsulfathiazole gives some promise when there are repeated recurrences in the presence of intestinal localization. In treatment of the acute or subacute brucella arthritides, azosulfamide and sulfathiazole have given splendid results.

It must be emphasized that there is no blanket method for treatment of all patients with brucellosis. Each patient presents an individual problem. Penicillin, or other mold derivatives, may ultimately prove to be the uniformly effective agent. To date, these preparations have given no promise of being effective in gram-negative bacillary infections, although early observations with penatin [17] (a protein antibacterial substance present in the crude filtrate of Penicillium notatum) were somewhat encouraging.

To date, the only commercially available preparations of brucella vaccine have been those containing the abortus and suis, or abortus and melitensis strains, or all three strains of the brucella. These may give undue reactions in cutaneous tests and in therapy. There is definite evidence that they have less effect in stimulating specific resistance than does the abortus strain alone, even in the presence of infections with Br. melitensis.[18] Recently a manufacturer of biologic preparations arranged to market a heat-killed Br. abortus vaccine, to be prepared from the same strain, of human origin, as the vaccine now prepared by the division of laboratories and research of the New York state department of health. When used in proper dilutions this vaccine should go a long way toward solving the problem of treatment in most cases of chronic brucellosis. Another manufacturer of biologic preparations has prepared the abortus strain of vaccine alone for the past several years, on special order.

In conclusion, I should like to express disagreement with the popular concept "that brucellosis is a rare disease and that there is no known method of treatment, in any event."

17. Kochalaty, W.: Personal communication to the author, March 1944.

18. Calder, R. M.: Chronic Brucellosis, South. M. J. **32**:451-460, 1939.

# SULFADIAZINE IN TREATMENT OF DACRYOCYSTITIS OF THE NEWBORN

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The treatment of simple epiphora or epiphora complicated by dacryocystitis occurring soon after birth is based on the premise that an obstruction is present at some point along the nasolacrimal duct. The types of obstruction may well be considered as (1) anatomic and (2) accidental.

The anatomic obstructive agent has been observed to be (1) an incomplete or delayed perforation of a thin membrane separating the lower end of the duct from the inferior meatus or (2) a congenital narrowing of the duct or a stricture in the canaliculus or at the entrance or exit of the lacrimal sac or within the nasolacrimal duct. It is difficult to see how employment of anything short of mechanical means would be logical treatment in a case of dacryocystitis resulting from an anatomic obstruction. In a case of this type, therefore, failure to effect a cure by digital pressure, supplemented in certain instances by irrigation of the sac and the use of simple antiseptics, has generally been considered an indication for probing. It is well known that digital expression of the sac and probing when indicated leads to cure of the infection and recovery of function in the vast majority of cases.

It is possible, however, that consideration of the disease on the basis of an accidental etiologic factor might lead to the employment of even more conservative, and newer, methods of treatment, which involve little risk and offer a reasonable chance of success. Furthermore, if an anatomic obstruction were always the cause of the dacryocystitis, there obviously would be few instances of spontaneous recovery and few reports of effective treatment by medical methods, including chemotherapy.

The accidental causes of epiphora and dacryocystitis in the newborn are (1) accumulations of epithelial, mucoid or mucopurulent material, forming plugs within the nasolacrimal duct or on the floor of the nose under the middle portion of the inferior turbinate or (2) inflammation and edema of the nasolacrimal duct secondary to nasal infection. A review of the literature and the results of medical treatment in the 2 cases here reported indicate that such causes as accumulations in the nasolacrimal duct or infection should be considered when treatment is undertaken. Larsson [1] called attention to the frequency of spontaneous cure, which emphasizes the possibility of accidental etiologic factors, and cited Comberg and Riser as asserting that a spontaneous rupture of the thin membrane blocking the lower end of the duct has been known to occur four months after birth. Judge [2] emphasized how frequently a collection of secretion and epithelial debris in the inferior meatus obstructs the nasolacrimal duct and is the cause of chronic dacryocystitis in the newborn. He urged the removal of this material by suction or cleansing as part of the initial treatment in all cases. He attributed the spontaneous recovery of dacryocystitis in the newborn to clearance of the inferior meatus by sneezing. Edwards [3] expressed the belief that the obstructions seen in the newborn were frequently due to clumps of epithelial cells or mucoid plugs within the duct or in the region of the inferior turbinate and suggested that pressure exerted through the sac would remove the obstructing substance. Hardesty [4] reported having carried out treatment in 60 cases of tearing in the very young during the preceding five years. In 34 per cent recovery was spontaneous, and in 66 per cent at least one probing was required. He made a plea for timely treatment, anticipating the probability of infection if simple epiphora was allowed to go on unchecked. He emphasized that drainage was seldom established after infection had occurred without at least repeated irrigations. It has been generally recognized, and the belief was expressed again in an article by Walker,[5] that a stricture in the canaliculus gives rise to uncomplicated

1. Larsson, S.: On Treatment of Congenital Atresia of Nasolacrimal Duct, Acta ophth. **16**:271, 1938.

2. Judge, H. V.: Dacryocystitis of Newborn, New York State J. Med. **41**:25 (Jan. 1) 1941.

3. Edwards, D. L.: Remarks on Treatment of Dacryocystitis, J. Oklahoma M. A. **32**:199 (June) 1939.

4. Hardesty, J. F.: Obstruction of Lacrimal Passages in Newborn Infant, J. Missouri M. A. **38**:40 (Feb.) 1941.

5. Walker, J. D.: Stenosis of Nasolacrimal Duct, Texas State J. Med. **37**:544 (Dec.) 1941.

epiphora, whereas obstruction lower down in the nasolacrimal duct might promptly be followed by infection of the sac, with persistence of chronic dacryocystitis, unless the flow of tears were reestablished. Reeder [6] stated the belief that in the congenital type of chronic dacryocystitis there was, as a rule, just a mucous or an epithelial plug in the nasolacrimal duct, and he urged irrigation of the duct with isotonic solution of sodium chloride. Harman,[7] in discussing the treatment of minor conditions of the eye, called attention to the fact that epithelial debris generally blocked the duct, and he seemed satisfied that medical measures usually cured the condition. Morgan [8] reported having seen 3 infants a few days old in whom there developed a tense swelling over the lacrimal sac which persisted a few days and spontaneously disappeared. He advocated digital massage, syringing of the duct and, when necessary, probing. These men are but some of the authors who have suggested that there are factors in the dacryocystitis of the newborn other than anatomic obstruction; the opinion has repeatedly been expressed that epithelial and mucous plugs either in the duct or on the floor of the nose should be recognized as frequent causes of congenital epiphora and dacryocystitis. It is probable that the epithelial plug referred to is related to the canalization of the nasolacrimal cord; indeed, the plug itself probably represents a failure of the central epithelial cells to separate and become necrotic.[9] If the epithelial plug is formed during embryonic life, it is hardly to be considered as directly related to infection, and little absorption by chemotherapeutic drugs would be expected. This leaves, however, a group of cases in which infection is the exciting agent from the start. Whether the infection causes edema of the mucosa of the nasolacrimal duct, with impeded outflow of tears and dacryocystitis, or produces the same effect by fostering the formation of a mucoid plug should make no particular difference in the response of the dacryocystitis to chemotherapeutic drugs.

The frequent relief of dacryocystitis in the newborn by digital massage or syringing should not make the case against infection as a primary cause any stronger, for it is easy to see that infection in the duct system may bring about a mucoid plug which is removed by digital pressure or syringing and the infection takes care of itself. The acceptance, therefore, of the thesis that infection may of itself cause the obstruction in the nasolacrimal duct or be the means whereby a mucopurulent plug may develop will tend to rationalize medical treatment for a condition which is generally regarded as surgical. In any event, infection is responsible for the mucous, and later the mucopurulent, secretion which follows blocking of the tears from any cause; and the least that can be expected from a trial of chemotherapy is clearing up of the infection, and then the obstruction, if anatomic, can be dealt with by probing. The success which followed the giving of sulfadiazine in the 2 cases reported here seems more than accidental and tends to modify one's understanding of the development of dacryocystitis in the newborn.

## REPORT OF CASES

CASE 1.—L. M. S., a white girl aged 7 months, was seen for the first time on Feb. 1, 1944. The mother stated that the baby's eyes were normal until late in December. The right eye began to tear, and an abscess of the lacrimal sac developed rapidly, with spontaneous rupture within a week. The edema over the sac and eyelids had considerably improved during the preceding month; but the discharge had not disappeared, and there was moderate brawniness over the inner portion of the lower lid. Examination on February 1 revealed three draining sinuses over the area of the right lacrimal sac, with considerable surrounding induration and redness. A small quantity of pus could be expressed from the sinus openings, which evidently led into the lacrimal sac. There were moisture and mucus at the inner canthus, but pus could not be expressed from either punctum. Unfortunately, no smear was made or material taken for culture at that visit. The mother was ordered to give the baby 0.5 Gm. of sulfadiazine at once and 0.25 Gm. every four hours for the next three days, except for one dose at night. The mother stated that within forty-eight hours the sinuses had healed over and no pus could be expressed from them. The baby was examined in seventy-two hours; already the redness and induration of the skin were decreased, and there was no epiphora. It was evident that the chronic dacryocystitis was healing rapidly. Administration of sulfadiazine was continued for another twenty-four hours. No blood count was made, and the amount of the sulfonamide compound in the blood was not determined. No other treatment was given except for cleansing of the skin, and a thin application of an ointment containing 5 per cent sulfathiazole, 25 per cent hydrous wool fat and 75 per cent petrolatum was made every few hours to the sinus openings until they healed. The child has been examined a few times since her recovery, the last examination being on June 8, and she is perfectly well. The important features of the case are the absence of epiphora and the almost complete absence of scarring or redness over the area of the sac. No pus, mucus or moisture could be expressed from either punctum at the last visit.

CASE 2.—T. M., a white boy aged 5 months, was seen March 7, 1944. The mother stated that the baby's eyes were entirely normal until he was 2 months of age.

6. Reeder, J. E., Jr.: Surgical Treatment of Chronic Dacryocystitis, J. Iowa M. Soc. **32**:15 (Jan.) 1942.

7. Harman, N. B.: Treatment of Minor Conditions in Eye, Brit. M. J. **1**:861 (April 16) 1938.

8. Morgan, O. G.: Observations on Treatment of Epiphora, Tr. Ophth. Soc. U. Kingdom **58** (part 1):163, 1938.

9. Riser, R. O.: Dacryostenosis in Children, Am. J. Ophth. **18**:1116 (Dec.) 1935.

At that time the left eye began to tear, and the onset was followed by a mucous, and later a purulent, secretion. The tearing and secretion had persisted, and the mother had been advised to employ digital expression of the sac and to keep the conjunctival sac free from any accumulation of secretion. Examination on March 7 revealed chronic inflammation of the left lacrimal sac. Considerable mucus and pus could be expressed from the sac, and there was a good deal of moisture at the inner canthus. A smear and culture of the secretion showed a pure growth of Staphylococcus aureus haemolyticus. The mother was advised to continue emptying the lacrimal sac by massage twice a day and to keep the conjunctival sac clean with a solution of boric acid. In addition, 0.5 Gm. of sulfadiazine was ordered to be given at once and 0.25 Gm. every four hours, except for one dose at night. Two days later the baby seemed much improved. The mother stated that for the first time in two months there had been no secretion in the conjunctival sac, and none could be expressed from the lacrimal sac. At the end of four days the dacryocystitis was entirely cured, and administration of sulfadiazine was discontinued. The baby has been seen regularly up to the time this paper was prepared, and there has been no recurrence of the symptoms. The important feature is the complete absence of epiphora.

## COMMENT

Numerous articles concerning the use of the sulfonamide compounds for ophthalmic conditions have appeared in the literature during the last seven years. References to the use of the drugs in treatment of disease of the lacrimal sac, however, have been more casual than the subject merits, and few cases have been reported in the American journals. Marshall [10] was one of the first investigators to estimate the level of a sulfonamide compound in body fluids and in body cavities after oral administration of the drug, and he proved that the substance did appear in empyema fluid in the pleural cavity. The earliest clinical summary of the use of sulfonamide compounds for ocular conditions was made by Hageman,[11] who reported on employment of sulfanilamide in treatment of gonorrheal conjunctivitis. Larsson [1] outlined the treatment of congenital atresia of the nasolacrimal duct but did not mention the use of chemotherapeutic drugs. Arruga [12] confined his article to the surgical treatment of lacrimation and inferred that any means of treatment other than surgical was generally ineffective. Jones [13] discussed the increasing help received from the sulfonamide compounds in management of diseases of the eye but did not refer to their use with infection of the lacrimal sac. The earliest report on the use of sulfanilamide in cases of dacryocystitis was by Castelli,[14] in 1939. Redslob and his associates [15] commented favorably on treatment with sulfapyridine in 9 cases of pneumococcic dacryocystitis. Excellent summaries, in which it was made clear that the sulfonamide compounds were of considerable assistance in ophthalmology, were published later in 1939 and 1940,[16] but in none of these articles did the authors mention their having had experience with the sulfonamide derivatives in cases of dacryocystitis. Edwards,[3] presenting the treatment of dacryocystitis, ventured the opinion that sulfanilamide should be used in treatment of acute dacryocystitis and would be expected to assist in aborting an acute attack. Adler and McDonald [17] recommended the internal use of the sulfonamide compounds in cases of acute suppurative dacryocystitis; they also employed the crystals of sulfadiazine locally in the sinus tracts after rupture of an acutely inflamed sac through the skin. Guyton and Woods,[18] in their last review from the Wilmer Institute, reported prompt healing of acute dacryocystitis due to the Koch-Weeks bacillus when sulfanilamide was used. Landegger [19] had not employed sulfanilamide in any case of disease of the lacrimal sac when he summarized his clinical experience in 1941. Goar [20] mentioned having insufflated sulfathiazole powder into a lacrimal fistula before operation, with good results. In the article previously referred to by

10. Marshall, E. K., Jr.: Determination of Sulfanilamide in Blood and Urine, J. Biol. Chem. **122**:263 (Dec.) 1937.

11. Hageman, P. O.: Clinical Experience in Use of Sulfanilamide at New Haven Hospital, J. Pediat. **11**: 195 (Aug.) 1937.

12. Arruga, H.: Surgical Treatment of Lacrimation, Arch. Ophth. **19**:9 (Jan.) 1938.

13. Jones, C. C.: Use of Sulfanilamide in Otolaryngology and Ophthalmology, J. Iowa M. Soc. **29**:6 (Jan.) 1939.

14. Castelli, A.: La para-aminofenilsulfamide nelle dacriocistiti, Boll. d'ocul. **18**:523 (July) 1939.

15. Redslob, E.; Marx, P.; Dieffenbach, P., and Milaras, T.: Essai de chimiothérapie des affections gonococciques et pneumococciques de l'appareil visuel, Bull. Soc. d'opht. de Paris **51**:326 (April) 1939.

16. Guyton, J. S.: Use of Sulfanilamide Compounds in Ophthalmology, Am. J. Ophth. **22**:833 (Aug.) 1939. Pryor, W. R.: Sulfanilamide: Its Effect on Eye, Ear, Nose and Throat, Kentucky M. J. **37**:305 (July) 1939. Glover, L. P.: Some Use of Sulfanilamide in Ophthalmology, Am. J. Ophth. **22**:180 (Feb.) 1939. Rutherford, C. W.: Sulfanilamide and Neoprontosil: Recent Advance in Ophthalmic Therapeutics, J. Indiana M. A. **33**:241 (May) 1940. Woodruff, H. W.: Sulfanilamide in Ophthalmology, Illinois M. J. **78**:418 (Nov.) 1940. Sykes, C. S.: Sulfanilamide in Ophthalmology, Texas State J. Med. **35**:780 (March) 1940.

17. Adler, F. H., and McDonald, P. R.: Paper read before the College of Physicians of Philadelphia, 1941.

18. Guyton, J. S., and Woods, A. C.: Advances in Use of Sulfanilamide Compounds in Ophthalmology, Am. J. Ophth. **24**:428 (April) 1941.

19. Landegger, G. P.: Sulfanilamide in Ophthalmology, California & West. Med. **55**:200 (Oct.) 1941.

20. Goar, E. L.: Evaluation of Recent Therapeutic Agents in Ophthalmology, Tr. Am. Acad. Ophth. **46**: 19 (Sept.-Oct.) 1941.

Walker,[5] in which he discussed the symptoms and treatment of stenosis of the lacrimal duct, he presented 2 cases of congenital dacryocystitis in which sulfapyridine was given. In the first case, that of a baby 5 months old with a pneumococcic infection of the sac, sulfapyridine was given, but the infection was not brought under complete control until a probe was passed. In the second case, that of a baby 3 weeks old with pneumococcic infection of both sacs, in spite of the use of sulfapyridine, irrigation of the lacrimal duct and local application of silver nitrate, each sac required probing for reestablishment of proper function and clearing up of the infection. During 1942 Heath,[21] Rutherford,[22] Scott [23] and Bellows [24] reported their experiences with use of the sulfonamide compounds but evidently they had not employed any of the compounds in treatment of diseases of the lacrimal sac. Braley,[25] in listing ocular conditions with their specific etiologic organism, recommended the oral administration of sulfadiazine or sulfathiazole for dacryocystitis caused by Staphylococcus aureus, the pneumococcus, Streptococcus haemolyticus and Friedländer's bacillus. Kolmer,[26] in a general discussion of chemotherapeutic drugs, said: "The sulfonamide compounds should be worthy of use in the treatment of dacryocystitis." Sorsby [27] reported the use of sulfapyridine in 2 cases of acute dacryocystitis in which incision was required. The organisms responsible were the Koch-Weeks bacillus and the pneumococcus respectively. Sorsby seems to have concluded that the sulfonamide therapy was helpful but that the abscess required drainage. In a review of the literature preceding the report of his cases, Sorsby did not mention any reference to the use of sulfonamide drugs in the treatment of dacryocystitis. Spaeth [28] suggested the direct injection into the sac of sulfathiazole or its sodium salt as a means of treatment of dacryocystitis. Leopold and Scheie [29] used a 5 per cent suspension of the microcrystalline form of sulfapyridine or sulfathiazole for treatment in 7 cases of dacryocystitis. In the first 5 cases the pneumococcic infection cleared rapidly after three daily injections of 2 cc. each of a 5 per cent suspension of sulfathiazole. The cultures were then sterile, and subsequently the obstruction in the lacrimal duct system was taken care of by additional means. In the sixth case, one of purulent dacryocystitis caused by the pneumococcus and the influenza bacillus, two injections of a 5 per cent suspension of sulfapyridine killed the pneumococcus, but even additional injections of sulfapyridine, and later sulfathiazole and sulfadiazine, failed to remove the influenza organism. In the seventh case an infection caused by the hemolytic streptococcus responded rapidly to two injections of sulfanilamide after injections of sulfapyridine had failed. The authors conclude that local injections into the sac of the sulfonamide compounds may prove a satisfactory method of controlling purulent dacryocystitis, at least temporarily. Thygeson,[30] in an excellent review of the literature, which included certain instructions given to all medical officers of the United States Army,[31] stated that sulfadiazine appeared to be the best of the compounds for treatment of this condition. He advised the use of sulfadiazine in all cases of acute and chronic dacryocystitis due to beta hemolytic streptococci, and he reported a single case of his own in which the condition healed rapidly.

In most of the aforementioned articles experience with dacryocystitis in adults is cited, but the situation with congenital epiphora and dacryocystitis is not so different that such information is not of considerable importance. There seems to be no dissenting opinion as to the usefulness of the sulfonamide compounds in treatment of dacryocystitis, and as the best drug to be used, with its dosage and route of administration, becomes established, this type of treatment will be more commonplace. A certain restriction, as to the route of administration of the drug at least, is placed on the treatment by the

21. Heath, P.: Some Uses of Chemotherapy in Ophthalmology, J. Michigan M. Soc. **41**:303 (April) 1942.

22. Rutherford, C. W.: Chemotherapy in Ophthalmology (Review of Recent Literature), J. Indiana M. A. **35**:697 (Dec.) 1942.

23. Scott, G. I., in Symposium on Chemotherapy in Ophthalmology, Tr. Ophth. Soc. U. Kingdom **62**:3, 1942.

24. Bellows, J. G.: Chemotherapy in Ophthalmology, Tr. Am. Acad. Ophth. **47**:19 (Sept.-Oct.) 1942.

25. Braley, A. E.: Sulfonamides in Treatment of Ocular Infections, Ohio State M. J. **38**:1101 (Dec.) 1942.

26. Kolmer, J. A.: Chemotherapy in Relation to Ophthalmology and Otolaryngology with Special Reference to Sulfonamide Compounds, Tr. Am. Acad. Ophth. **47**:36 (Sept.-Oct.) 1942.

27. Sorsby, A., in Symposium on Chemotherapy in Ophthalmology, Tr. Ophth. Soc. U. Kingdom **62**:15, 1942.

28. Spaeth, E. B.: Résumé of Sulfonamide Drugs in Ophthalmology, Pennsylvania M. J. **46**:566 (March) 1943.

29. Leopold, I. H., and Scheie, H. G.: Studies with Microcrystalline Sulfathiazole, Arch. Ophth. **29**:811 (May) 1943.

30. Thygeson, P.: Sulfonamide Compounds in Treatment of Ocular Infections, Arch. Ophth. **29**:1000 (June) 1943.

31. Chemotherapy in Infectious Diseases and Other Infections, United States War Department Circular Letter 17, Washington, D. C., Government Printing Office, May 1942.

age of the patient; so it is likely that direct injection of a sulfonamide drug in solution into the lacrimal apparatus in babies will have a rather limited application because the procedure is fairly formidable and is comparable to probing. Oral administration to babies, however, is simple because the drug can be given with the formula; even if this method failed, the satisfactory report of Leopold and Scheie [20] would compel one to try local injections. It has always been of scientific interest at least to determine the organism responsible for an infection of the sac. Such information is more important than ever now; so a direct smear should be made and material for culture taken at the initial visit. The information obtained will be of considerable value in treatment and prognosis. The most common organisms responsible for infection of the lacrimal sac are Staph. aureus haemolyticus, the pneumococcus, the beta hemolytic streptococcus, Koch-Weeks bacillus and Friedländer's bacillus. This group of organisms can be rather readily identified on smear and by culture and require no special mediums for growth. These organisms are all notably inhibited by the sulfonamide drugs except for the Koch-Weeks bacillus, and even this bacillus will at times respond to chemotherapy.[18] Experimental and clinical investigation has produced evidence that the pneumococcus and gonococcus are more sensitive to sulfathiazole, while sulfanilamide is more active against the streptococcus. It is possible that sulfadiazine and sulfamerazine (sulfamethyl diazine) are active to an equal degree against all the organisms mentioned.

## COMMENT

A review of the causes of congenital epiphora and dacryocystitis has shown that there is a factor of infection in all cases. This factor may be primary, in which case the entire process is dependent on bacterial invasion of the mucous membrane of the nose and the nasolacrimal duct. On the other hand, the infection may be secondary, in which case the underlying anatomic obstructive agent favored the development of infection by insufficient drainage of the tears. In this paper the emphasis is placed on the element of infection and its cure. When a case of congenital epiphora with dacryocystitis is seen for the first time, it is impossible to know whether an anatomic obstruction exists, and for that reason chemotherapy in conjunction with other conservative treatment is to be recommended in all cases. It is probable that such treatment, especially if instituted early, will result in surgical treatments being required in fewer cases. The success of the oral administration of the sulfonamide compounds or the local injection of their microcrystalline form in clearing up the infection has been demonstrated; a complete cure will be obtained in many cases, and in cases in which simple epiphora remains separate means can be taken to remedy that situation.

The additional conservative treatment suggested consists of such conventional means as cleansing of the inferior meatus by suction, irrigation of the nasolacrimal duct with isotonic solution of sodium chloride and digital pressure on the distended lacrimal sac, in an attempt to rupture a congenital membrane or stricture.

From a survey of the literature on the use of sulfonamide drugs in ophthalmology, it is evident that the use of sulfonamide compounds for dacryocystitis, especially of the congenital type, has not received the attention it deserves. It is possible that too much emphasis has been placed on a physical obstruction as the underlying factor in most cases of congenital dacryocystitis; even the digital pressure has been employed with the idea not of draining a chronic mucopurulent cavity but of rupturing an obstruction within the nasolacrimal duct by hydrostatic pressure. With the discovery of the increasing field of usefulness of chemotherapy, it is important that the drugs be employed in every disease of the eye or adjacent structures which offers the slightest chance of improvement.

## SUMMARY

In 2 cases of congenital dacryocystitis a satisfactory response was obtained with administration of sulfadiazine.

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# Clinical Notes

## ACCIDENTAL VACCINIA OF THE EYELID WITH DISCIFORM KERATITIS

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Accidental ocular vaccinia is rare. Since the days of Jenner few cases have been reported in the literature, and few physicians have had the opportunity of seeing a case. Such an accidental infection is seen first by the general practitioner, the family physician. It is proper therefore that the present case be reported. The diagnosis is problematic, but the history of vaccination of a member of the family will aid in recognition of the true nature of the condition. In reality the clinical picture is pathognomonic.

### REPORT OF A CASE

M. R., a girl aged 14, was referred to my service at the Jewish Hospital by her family physician with the diagnosis of hordeolum. Four days before the patient had gone to a picnic in the park. Two days later the left eye became red and the lid swollen. The family physician referred her to the hospital.

Examination revealed that the right eye was normal, with vision of 20/20. The eyelids of the left eye, both upper and lower, were notably swollen and inflamed. The conjunctiva was chemosed; photophobia was pronounced; the cornea was somewhat hazy and because of irritation could not well be examined. The preauricular glands were enlarged and somewhat painful to the touch. The patient offered the statement that vision in the left eye had been as good as that in the right eye prior to the infection.

On the margin of the left upper lid near the outer canthus was a large ulcerated area covered with a white film which looked like a pseudodiphtheritic membrane. A few eyelashes were missing. A smaller ulcer, covered likewise with a white membrane, was seen on the nasal side of the margin of the same lid. On the margin of the lower lid there were three small, circumscribed, flat ulcers covered by a thin yellowish membrane characteristic of vaccinial ulceration in that area. The conjunctiva, while chemosed, was not ulcerated. There was no purulent discharge. A smear and culture of material yielded Staphylococcus aureus. The clinical picture was puzzling, and I asked Dr. Erich Urbach, allergist, to examine the patient. In answer to his question whether any one in the family had been vaccinated, the mother replied that a younger sister, aged 6 years, had been vaccinated two weeks ago and had been sleeping with the patient. On the basis of this history and the clinical picture, we concluded that the case was one of accidental transfer of vaccinia to the lid.

The patient refused to go to the hospital and was permitted to return home, with instructions to carry out the following treatment: use of sodium sulfathiazole, 3 per cent, as an eye wash; instillation of atropine sulfate solution, 1 drop three times a day, and application of boric acid ointment at night. She was of course warned not to sleep with any one.

Appearance of left eye on tenth day of treatment.

She returned three days later, when the swelling of the lids was much reduced, but the corneal haze had developed into a typical picture of disciform keratitis. Vision was considerably reduced and photophobia more intense. After three months of treatment the ocular process became quiet, with only a disk-shaped opacity on the cornea—left to tell the story of the infection.

There is no specific treatment for this condition; the therapy is purely symptomatic. My patient was vaccinated at the age of 6 years but apparently, after eight years, had lost her immunity to smallpox, as evidenced by the accidental infection with vaccinia. It is possible that this accidental vaccinia has conferred a new period of immunity on the patient.

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†Dr. Brav died Dec. 2, 1944.

# Ophthalmologic Reviews

EDITED BY FRANCIS HEED ADLER

## OPTOCHIASMIC ARACHNOIDITIS

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### DEFINITION AND HISTORICAL REVIEW

One runs into difficulties at once in attempting to define optochiasmic arachnoiditis. The concept of this disease is gradually undergoing change; it is not today what it was, say twelve years ago, and I do not doubt that it will still evolve considerably. Even at present every one is not in complete agreement with regard to this condition.

I believe one may best approach the subject by outlining the several lines of converging thought by which the notion of optochiasmic arachnoiditis was arrived at. The first of these starts with acromegaly, which Pierre Marie,[1] in 1886, showed was due to a tumor of the pituitary gland. Such a tumor, later identified as acidophilic adenoma, grows upward, presses on the chiasm and causes visual disturbances, with bitemporal field defects. A few years later Babinski [2] proved that a pituitary tumor could be linked with a different clinical picture, eventually known as the Babinski-Fröhlich syndrome. A tumor producing such a condition, now known to be a chromophobic adenoma, could also produce bitemporal hemianopsia, and during the first quarter of this century neurologists and ophthalmologists came to accept the idea that bitemporal hemianopsia was due to a chiasmic lesion, and therefore to a pituitary tumor. With the improvement of neurosurgical technic, operations for intracranial tumor became more numerous, and it was realized that the optic chiasm could suffer damage not only from an intrasellar growth under it but, in some instances, from a suprasellar tumor located above and anterior to it. In 1929 Cushing and Eisenhardt [3] brought to the attention the meningiomas inserted on the tuberculum sellae, and after the thirteenth International Congress of Ophthalmology, held in Amsterdam in September 1929, it was generally accepted that a chiasmic syndrome with bitemporal hemianopsia could be produced not only by sellar but by suprasellar tumors. The next step followed at once, when it was understood that such bitemporal field defects could also result from pseudotumors, in the form of circumscribed collections of fluid, probably of inflammatory origin, occurring in the anterior, or perichiasmic, cistern. At the Amsterdam congress both Holmes [4] and Cushing [5] reported cases of such lesions.

The second train of thought leading to the concept of optochiasmic arachnoiditis started with Quincke, when he described generalized serous meningitis. A few years later Schlesinger [6] showed that in some cases circumscribed collections of fluid were observed. The first of such pseudotumors were seen in the spine, but shortly afterward localized pockets of serous meningitis were observed to form on the lateral surface of the hemispheres. It was already suspected that the underlying nerve tissue was not normal and was also affected by an inflammatory process. In the early twenties, when the cerebellopontile angle was more readily explored, operation was performed in several cases in which such circumscribed collections had formed in the posterior fossa and were mistaken for acoustic tumors. In 1924 Horrax [7] described cases of such collections of fluid; he concluded that they represented chronic adhesive or cystic

1. Marie, P.: Sur deux cas d'acromégalie, Rev. de méd. **6**:297 (April) 1886; in Travaux et mémoires, Paris, Masson & Cie, 1926, vol. 1, pp. 185-223.

2. Babinski, J.: Tumeur du corps pituitaire sans acromégalie et avec arrêt du developpement des organes génitaux, Rev. neurol. **8**:531-532, 1900.

3. Cushing, H., and Eisenhardt, L.: Meningiomas Arising from the Tuberculum Sellae, Arch. Ophth. **1**: 1-41 (Jan.); 168-206 (Feb.) 1929.

4. Holmes, G.: Suprasellar Tumors, Tr. Internat. Cong. Ophth., 1929.

5. Cushing, H.: The Chiasmatic Syndrome of Primary Optic Atrophy and Bitemporal Field Defects in Adults with a Normal Sella Turcica, Arch. Ophth. **3**:505-551 (May); 704-735 (June) 1930.

6. Schlesinger, H,: Beiträge zur Klinik der Rückenmarks- und Wirbeltumoren, Jena, G. Fischer, 1898.

7. Horrax, G.: General Cisternal Arachnoiditis Simulating Cerebellar Tumors, Arch. Surg. **9**:95-112 (July) 1924.

arachnoiditis and were the sequel of a meningoencephalitis which had left more or less circumscribed areas of adhesions between the arachnoid and the underlying patch of atrophied cortex, The next step came when it was realized that the anterior, or chiasmic, cistern could also be the site of such pockets; again, one comes to Cushing's paper, published in 1930,[5] in which he stated that if localized meningeal reactions can be produced in the cerebellopontile cistern by an inflammatory process in the middle ear, there is no reason that a similar process might not occur in the chiasmic cistern as a consequence of infection of the paranasal sinuses.

A third line of approach was followed by investigators who were more concerned with lesions of the optic nerves than those of the chiasm and had hoped that operation might relieve mechanical pressure or stricture in some cases. It was evidently this hope which prompted Balado to operate on a patient with bilateral primary optic nerve atrophy. A temporofrontal opening disclosed a milky appearance of the arachnoid, and the thickening of the arachnoid continued as far as the base and surrounded both optic nerves. Balado opened the thickened sheaths of the nerves and observed that they were thinned and abnormally pink. There was improvement of the field, and he and Satanowsky [8] reported the history of this patient in March 1929.

That year, 1929, was therefore a turning point, or one might say a point of convergence. From that time attention was focused on the possibility of the occurrence of such a case, and many were verified at operation. The papers published by Deery [9] and Frazier,[10] in 1930, and by Heuer and Vail,[11] Davis [12] and Craig and Lillie,[13] in 1913, are important landmarks in American medical literature. Since 1931, Vincent and his associates,[14] in France, have contributed repeatedly to knowledge of this syndrome, and numerous papers have been published in many countries.[15] Two points have gradually emerged as important: First, the field defects were not necessarily bitemporal, and, second, the visual impairment was often due not only to the meningeal lesions and consequent pressure on the optic nerves and chiasm but, to a great extent, to an inflammatory process in the visual pathway itself.

If I were to give my definition of optochiasmic arachnoiditis as I understand it today, I should say that in some cases, as a consequence of various infectious and possibly toxic noxae, a localized inflammatory process can be seen at the base of the brain which affects the chiasm and the optic nerves, as well as the meninges which surround them. The meningeal reaction can take different forms: veils, fibrous bundles, thickened sheaths and circumscribed collections of fluid. Although the meningeal lesions are the most apparent, the inflammatory changes in the underlying visual fibers are often no less essential. The relative importance of the meningeal and the nerve lesions is variable; this may have a bearing on the clinical picture, and possibly on the prognosis. The visual disturbance is not necessarily of the bitemporal type; central scotoma is frequent. In some cases, but in some only, operation will prove useful, but one is not able at present to select such cases. Knowledge is still in a state of flux, and it is likely that this syndrome will eventually be broken down as the etiologic factors are better understood and more is learned about the indications for surgical treatment.

## FREQUENCY

Statistical data do not give a true picture, since this disease is not widely known and its existence as an entity is not universally accepted. Some ophthalmologists and surgeons may see a greater number of cases than is normal because they are particularly interested in the syndrome. Others have failed to recognize the condition or have treated it with nonoperative procedures.

8. Balado, M., and Satanowsky, P.: Tratamiente quirúgico di la atrofia di la papila, Arch. argent. de neurol. **4**:71-75, 1929.

9. Deery, E. M.: Syndromes of Tumors of the Chiasmal Region, J. Nerv. & Ment. Dis. **71**:383-396, 1930.

10. Frazier, C. H.: Cerebral Pseudotumors, Arch. Neurol. & Psychiat. **24**:1117-1132 (Dec.) 1930.

11. Heuer, G. J., and Vail, D. T. Jr.: Chronic Cisternal Arachnoiditis Producing Symptoms of Involvement of the Optic Nerves and Chiasm, Arch. Ophth. **5**:334-349 (March) 1931.

12. Davis, L.: Chiasmal Syndrome in Intracranial Tumors, Arch. Ophth. **6**:181-210 (Aug.) 1931.

13. Craig, W. M., and Lillie, W. I.: Chiasmal Syndrome Produced by Chronic Local Arachnoiditis, Arch. Ophth. **5**:558-574 (April) 1931.

14. (*a*) Vincent, C.; David, M., and Puech, P.: A propos de sept cas d'arachnoïdite opto-chiasmatique, Rev. neurol. **1**:760-767, 1931. (*b*) Vincent, C.: Le traitement chirurgical des compressions directes du chiasma et du nerf optique dans le crâne, Bull. Soc. d'opht. de Paris, 1932, pp. 282-301. (*c*) Vincent, C.; Puech, P., and Berdet, H.: Les arachnoïdites de la base du cerveau, Rev. d'oto-neuro-opht. **14**:417-428, 1936.

15. (*a*) Malbran, J., and Balado, M.: Arachnoidis quiasmatica, Arch. argent. de neurol. **8**:96-106, 1933. (*b*) Morea, R.: Tratamiento quirugico de la atrofia de la papila, ibid. **7**:301-331, 1933. (*c*) di Marzio, Q.; Cavina, C., and di Negris, G.: Sulla arachnoidite opto-chiasmatica, Riv. oto-neuro-oftal. **13**:291-328, 1936.

so that the diagnosis has not been verified. With these reservations, the following figures are cited: In 1930 Deery [9] stated that of 170 cases of chiasmic and perichiasmic tumors and pseudotumors operated on in Cushing's service during the preceding ten years, 13 had been cases of optochiasmic arachnoiditis. In 1931 Heuer and Vail [11] found that in 5 per cent of 43 cases of optic nerve atrophy the condition was due to optochiasmic arachnoiditis. In 1938, when I was working in the ophthalmologic department of Vincent's neurosurgical service, I published, with Guillaumat,[16] a statistical report of all verified cases in which the eyes had been examined either in that department or in my private practice. My findings follow:

| | No. of Cases |
|---|---|
| All intracranial tumors, including those of the chiasmic region | 847 |
| Tumors of the chiasmic region | |
| Pituitary adenoma | 50 |
| Craniopharyngioma | 37 |
| Tumors of the chiasm | 16 |
| Other tumors | 6 |
| Total | 109 |
| Circumscribed pockets of serous meningitis on the outer surface of the hemispheres | 48 |
| Arachnoiditis of the posterior fossa | 35 |
| Optochiasmic arachnoiditis | 78 |

These figures show that optochiasmic arachnoiditis is not a rare disease, but the relative proportion is certainly too high, as previously stated, since Vincent and his co-workers were particularly interested in this disease. In 1937, Bollack, David and Puech,[17] the last two also associates of Vincent, published a book on optochiasmic arachnoiditis.[18] At that time they had found 63 reported cases, and they added to these 66 more previously unreported cases, making a total of 129 cases. These cases should not be added to those given in the tabulation, as many of the same cases are counted in the two series.

Optochiasmic arachnoiditis is more frequent in adult life; 60 per cent of cases occur between the ages of 20 and 40, with a maximum between the ages of 20 and 30. The findings of Bollack, David and Puech [17] follow.

| | No. of Cases |
|---|---|
| Between birth and 10 years of age | 7 |
| From 10 to 20 | 12 |
| 20 to 30 | 37 |
| 30 to 40 | 35 |
| 40 to 50 | 27 |
| Over 50 | 6 |
| | 124 |
| Men affected | 77 |
| Women affected | 46 |
| | 123 |

### PATHOLOGIC FEATURES

To facilitate the description of the lesions encountered, one may, rather artificially, separate them into three types: thickening and adhesions of the arachnoid; circumscribed collections of fluid, and atrophy of the optic nerves and chiasm. One should, however, bear in mind that any one of these three types of lesions rarely occurs alone but merely predominates and that the relative proportion is variable.

1. *Thickening of the Arachnoid and Adhesions.*—The arachnoid is thickened and encases the optic nerves and the optic chiasm more or less completely. It forms adhesions both with the visual pathway and with the surrounding organs, in particular the cortex, the olfactory nerves and the perichiasmic blood vessels (internal carotid, anterior cerebral, anterior communicating and ophthalmic arteries). There is notable vascularization of the thickened arachnoid. The veins are sometimes extremely dilated, pointing to impairment of the return circulation. Occasionally one sees small calcareous deposits. The arachnoid sometimes forms a continuous milky veil or a heavy membrane. In other cases innumerable short, fine, cobweblike adhesions are attached to the chiasm and the optic nerves. In other cases strong, thick fibrous bundles bridge the perichiasmic region; most of these seem to originate from the neighboring arteries, the internal carotid and the ophthalmic artery in particular, and in many cases they form strictures of the optic nerves and the optic chiasm, which may be deeply grooved. Such strictures may also be due to the fact that the anterior cerebral or the anterior communicating artery is drawn away from its normal course and bound down by arachnoid adhesions.

*Circumscribed Pockets of Subarachnoid Fluid.*—Circumscribed pockets of serous meningitis in the perichiasmic region may closely simulate a tumor both in their appearance and in the way

16. Hartmann, E., and Guillaumat, L.: Aspect du fond d'oeil dans les tumeurs intracraniennes, Ann. d'ocul. **75**:717-737, 1938.

17. Bollack, J.; David, M., and Puech, P.: Les arachnoïdites optochiasmatiques, Paris, Masson & Cie, 1937.

18. I have made considerable use of this book not only because it is the most complete survey of optochiasmic arachnoiditis but because I had personally examined most of the patients forming the material of this work.

they bring pressure on the visual pathway. The pocket is suprasellar, and usually above and anterior to the chiasm, but it has sometimes been seen under the chiasm and the optic nerves. In other cases there is not one large pocket but innumerable small ones.

*Atrophy of the Visual Fibers.*—The optic nerves and optic chiasm are rarely normal. They usually show more or less pronounced atrophy; the nerves, in particular, may be reduced in caliber and in some instances flattened. Less frequently one may see enlarged optic nerves, giving the impression of being edematous and appearing to be strangulated at the optic foramen. Their color is rarely normal, being at times grayish white, sometimes of a gelatinous appearance, and at other times notably congested, with excessive vascularization of the surface. While in some cases the atrophy of the visual pathway seems to be a consequence of the constrictions exerted by the thickened arachnoid or by a pseudotumorous pocket of serous meningitis, in other cases the meningeal lesions are so discrete and the atrophy of the optic nerves so pronounced that one has the impression, rather, of a primary inflammatory process of the nerves.

There are few satisfactory reports of the microscopic lesions. Davis and Haven [19] in 2 cases noted that there were prominent thickening of the reticular structure, due to an increase in the fibrous elements, and a moderate amount of leukocytic infiltration of this reticular area. Bollack, David and Puech [17] reported 2 cases in which the optic nerves and optic chiasm were examined: There was peripheral neuritis with demyelination and atrophy of some of the more superficial nerve fibers.

## ETIOLOGIC FACTORS

It has long been known that in some cases a localized area of arachnoiditis may cover an underlying tumor, and this may occur in the chiasmic area, as well as on the outer surface of the hemispheres; but I shall not discuss this type of peritumoral arachnoiditis here.

In the present state of knowledge no one etiologic factor is evident. Rather, one gathers the impression that optochiasmic arachnoiditis can be caused by several infectious, and possibly some toxic, noxae. The most comprehensive statistics are those cited by Bollack, David and Puech.[17] I have tabulated the etiologic agents suspected in the 63 cases reported in the literature prior to their publication and the causal factors in the 66 previously unpublished cases which they reported. The second group of cases is more interesting, as a possible etiologic agent was found in a greater percentage of cases than in the first group.

| | Previously Published Cases | Unpublished Cases | Total No. of Cases |
|---|---|---|---|
| Total no. of cases | 63 | 66 | 129 |
| Total no. of possible causes found | 28 | 53 | 81 |
| Trauma of the skull or orbit | 9 | 10 | 19 |
| Diseases of the nose, sinuses and tonsils | 7 | 10 | 17 |
| Syphilis | 3 | 9 | 12 |
| Otitis | 2 | 4 | 6 |
| Tuberculosis | 1 | 4 | 5 |
| Familial disease | 1 | 3 | 4 |
| Rheumatic fever | 0 | 3 | 3 |
| Teeth | 2 | 0 | 2 |
| Encephalitis | 1 | 1 | 2 |
| Pregnancy | 1 | 1 | 2 |
| Influenza | 0 | 2 | 2 |
| Infection with colon bacillus | 0 | 2 | 2 |
| Herpes zoster (intercostal) | 0 | 1 | 1 |
| Cerebrospinal meningitis | 1 | 0 | 1 |
| Typhus | 0 | 1 | 1 |
| Diabetes | 0 | 1 | 1 |
| Erysipelas | 1 | 0 | 1 |
| Alcoholism | 0 | 1 | 1 |
| Mumps | 1 | 0 | 1 |

One should bear in mind that this classification is only tentative, and an infectious disease reported in the patient's history previous to his visual disturbance implies no certainty as to its causative action. In several cases two possible causes were reported, such as infection of the teeth and nose, infection of the nose and sinuses, infection of the sinuses and trauma, tuberculosis and trauma and nasal infection and otitis. Some of these etiologic possibilities should be considered more carefully, namely infections of the sinuses and nose, trauma and syphilis.

*Infection of the Nose and Sinuses.*—When reporting one of the first cases in 1929, Cushing [5] stated:

> . . . That a mild meningeal reaction may be produced in the cerebellopontile cisterna by an inflammatory process in the middle ear with symptoms suggesting those of an acoustic tumor, is well known. There is no reason . . . why a similar process might not occur in the chiasmal cisterna in association with inflammatory processes in the accessory paranasal sinuses [page 730].

Such an etiologic factor was also accepted as probable by Monier-Vinard; [20] by Puech, David

19. Davis, L., and Haven, H. L.: Pathologic Study of the Intracranial Arachnoid Membrane, J. Nerv. & Ment. Dis. **73**:129-143 and 286-300, 1931.

20. Monier-Vinard, M., in discussion on Puech, P.; David. M., and Brun, M.: Rev. d'oto-neuro-opht. **11**: 621, 1933.

and Brun,[21] and by Vail.[22] In 1936 Worms [23] reported an interesting case history. His patient had a long-standing infection of the sphenoid sinuses, with polyps, and osteitis of the posterior wall; a perforation occurred eventually, and the patient died. Postmortem examination disclosed conspicuous perichiasmic arachnoid membranes. But this is a rather unusual occurrence. More often the symptoms are less acute, and only a relatively moderate and subacute or chronic inflammatory process is seen. Also, the initial infection need not be in the sinuses; a chronic infection of the postnasal cavity or of the tonsils may be a sufficient cause. The lymphatic channels of the nose are known to be directly related to the subarachnoid spaces, and there is also an anastomosis linking the veins of the sphenoid sinuses and the ethmoid cells to the ophthalmic veins and to small veins originating in the dural sheaths of the optic nerve in the optic canal. Either of these channels might be responsible for inflammatory arachnoiditis, even without fissures of the bones. Infections of the nose and sinuses are so frequent, however, that arachnoiditis may well occur in a patient previously a victim of such trouble without this being the real cause.

*Trauma.*—It is usual for a patient to find a traumatic explanation for almost any disease, and more or less severe trauma to the head is so frequent an occurrence, even with normal people, that such a history in the case of a patient with arachnoiditis is not necessarily significant. Some cases, however, are suggestive in particular, the case reported by Weill,[24] in which symptoms of adenoma of the pituitary were present and operation, performed by Vincent, revealed optochiasmic arachnoiditis, with fibrous tracts starting from the vault at the site of a scar of the epineurium and the skin. The patient had previously had an automobile accident, resulting in an injury to the head. In 1 of the first cases reported, case 1 of Holmes,[4] there had been a trauma to the skull, and in several other cases the condition has been ascribed with more or less certainty to a head injury (Malbran and Balado;[15a] Morea;[15b] di Marzio, Cavina and di Negris;[15c] Heuer and Vail,[11] and others).

Bollack, David and Puech [17] found 10 cases of head trauma in their series of 66 cases of this form of arachnoiditis, and in 6 cases the trauma was the only likely etiologic factor; in 4 cases other causes were present (syphilis, tuberculosis and nasal or sinal infection). In 1939 Kenel [25] reported 5 cases of optochiasmic arachnoiditis of traumatic origin, in 4 of which operation was performed.

It is evident, therefore, that a head trauma must be accepted as a possible cause of optochiasmic arachnoiditis, and this may have important legal implications. If the arachnoiditis followed shortly the head injury, the link is evident; but the visual disturbance may be a late symptom, and in such cases doubt may persist, especially if the trauma was moderate or if some other possible etiologic factor is present, such as syphilis or sinusitis.

*Syphilis.*—There is no general agreement as to the part played by syphilis. A priori reasoning might lead one to accept this type of infection as a frequent cause since one knows how often chronic meningitis with optic nerve atrophy follows insufficiently treated syphilis. However, cases of this type are more usually classified with tabes, and the condition differs from the disease I am discussing in this review. But it is certain that patients with optochiasmic arachnoiditis sometimes have a history of syphilis.

In Cushing's first case [5] (1929) the serologic reaction was suspected of being positive, and similar cases have been reported by François,[26] MacPherson [27] and Schaub.[28] In 1936 Vincent, Puech and Berdet [14c] claimed that in 2 out of 5 of their cases the Wassermann reaction of the blood was positive. Of their 129 cases, Bollack, David and Puech [17] reported on the Wassermann reaction of the blood in only 78: It was positive in 12 and negative in 66 cases, the Kahn reaction being positive in 1 of the latter. Hausman [29] especially stressed the importance of syphilis in arachnoiditis. In 1937 he reported 5 cases, and in 1940 he gave his observations in 15 cases of syphilis and diseases of the optic nerves occurring

21. Puech, P.; David, M., and Brun, M.: Contribution a l'étude des arachnoïdites opto-chiasmatiques, Rev. d'oto-neuro-opht. **11**:641-649, 1933.

22. Vail, D.: Optochiasmatic Arachnoiditis, Arch. Ophth. **20**:384-394 (Sept.) 1938.

23. Worms, G.: Syndrome oculo-hypophysaire consécutif à une sinusite sphénoïdale suppurée, Arch. d'opht. **53**:207-217, 1936.

24. Weill, G., in discussion on Les arachnoïdites optochiasmatiques, Bull. et mém. Soc. franç. d'opht. **54**:198, 1937.

25. Kenel, C.: Five Cases of Traumatic Optochiasmatic Arachnoiditis, Ophthalmologica **96**:345, 1939; abstracted, Am. J. Ophth. **22**:811, 1939.

26. François, J.: Arachnoïdite optochiasmatique syphilitique et pyrétothérapie, Bull. et mém. Soc. franç. d'opht. **50**:185-189, 1937.

27. MacPherson, W. A.: Chiasmal Arachnoiditis, Am. J. Ophth. **23**:1275-1276, 1940.

28. Schaub, C. F.: Syphilitic Optico-Chiasmatic Arachnoiditis, Am. J. Ophth. **24**:1313, 1941.

29. Hausman, L.: Syphilitic Arachnoiditis of the Optic Chiasm, Arch. Neurol. & Psychiat. **37**:929-958 (April) 1937; Syphilitic Atrophy of the Optic Nerves and Papilledema Due to Optochiasmatic Arachnoiditis: Indications for Surgical Intervention, Arch. Ophth. **23**: 1107-1115 (May) 1940; The Surgical Treatment of Syphilitic Optic Nerve Atrophy Due to Chiasmal Arachnoiditis, Am. J. Ophth. **24**:119-132, 1941.

in the service of Dr. Foster Kennedy: 1 case of papilledema, 1 case of secondary optic nerve atrophy and 13 cases of primary optic nerve atrophy. In 4 cases the chiasmic region was explored, 3 being cases of the primary type of optic nerve atrophy and 1 a case of secondary optic nerve atrophy. In the first 3 cases adhesions were present around the chiasm; these were removed, and vision improved. The patient with secondary optic nerve atrophy had internal hydrocephalus, and his condition did not improve.

My associates and I [30] have reported the history in a case of tabes with altitudinal hemianopsia, an unusual complication of this disease; operation disclosed that a thick veil of arachnoid adhesions had pulled the anterior cerebral artery away from its normal course and bound it down against the superior aspect of the chiasm, which was deeply grooved. That syphilis plays a part in the causation of optochiasmic arachnoiditis is certain, but arachnoiditis is far from being due to syphilis in all cases, and operation should not be performed in all cases of optic nerve atrophy complicating syphilis. In this matter the ophthalmologist should use his judgment.

One should also bear in mind that in a syphilitic patient, even with a positive Wassermann reaction of the blood, arachnoiditis may be due to some other cause. Of the 12 cases in which Bollack, David and Puech [17] reported a positive Wassermann reaction of the blood, a dental infection was also present in 1, diabetes in 1, trauma to the frontal area in 1 and chronic nasal infection in 2. Arachnoiditis in a syphilitic patient is not necessarily of syphilitic origin.

### MECHANISM OF THE VISUAL SYMPTOMS

When the first cases of optochiasmic arachnoiditis were reported, it was considered evident that the optic chiasm and the optic nerves suffered from direct pressure, that circumscribed collections of fluid acted as would a solid tumor and that thickened membranes or fibrous bundles were noxious because of constriction of the visual fibers. Such an explanation is still accepted in a great number of cases, but it has gradually become apparent that it did not suffice in a series of other cases. Pressure on or constriction of the optic nerves and chiasm is sometimes of moderate degree, in contrast to the abnormal, and often atrophic, appearance of the nerves. The importance of the inflammatory process in the visual pathway has been increasingly emphasized, and the present tendency is to consider optochiasmic arachnoiditis not as a disease of the arachnoid, with secondary mechanical damage to the nerve fibers, but as an inflammatory process involving the arachnoid and the nerve fibers in variable proportions. Some authors have concluded that the inflammatory process occurs simultaneously in the two structures; others have stated the belief that it begins in the meninges and spreads to the optic nerves and the optic chiasm, and some investigators have asserted that it more often originates in the visual pathway and that the arachnoiditis is a secondary reaction.

It cannot be overlooked, moreover, that the visual fibers may suffer from an impaired blood flow. It has often been noted that the arachnoid adhesions exerted a traction on the arteries from which the chiasm and optic nerves derived their supply and that in some patients the veins were notably congested, as though there was an obstacle to the return circulation. The normal nutrition of the nerve fibers might therefore be altered by mechanical ischemia, by a reflex spasm (Sourdille [31]) or by venous stasis. This venous engorgement is worth noting at a time when there is a tendency to consider multiple sclerosis and the other demyelinating diseases as noninfectious and as due to venous thrombosis (Putnam [32]). Vail [22] stated that encephalitis, multiple sclerosis and optochiasmic arachnoiditis were closely allied and might be different manifestations of the same pathologic process, which could well be thrombosis of the venous system of the nerve tissue.

It is reasonably certain that no single mechanism is responsible and that several factors may produce the visual disturbance, either in different patients or in the same patient, the relative importance of these mechanisms being variable.

### SYMPTOMS

*Field Defects.*—In most of the early cases bitemporal field defects were recorded. This was only natural since at first optochiasmic arachnoiditis was usually encountered at operation in cases in which a tentative diagnosis of adenoma of the pituitary or suprasellar tumor had been made. It gradually became evident, however, that bitemporal hemianopsia was not the only type of field defect and, in fact, was not even the most frequent.

30. David, M.; Hartmann, E., and Hebert, E.: Arachnoïdite et compression vasculaire du chiasma chez un tabétique, Bull. Soc. d'opht. de Paris, 1936, pp. 789-798.

31. Sourdille, G. P.: Utilité d'une thérapeutique extracranienne au stade début de l'arachnoïdite, Bull. et mém. Soc. franç. d'opht. **50**:181-184, 1937.

32. Putnam, T. J.: Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," Arch. Neurol. & Psychiat. **37**:1298-1321 (June) 1937; Multiple Sclerosis and Encephalomyelitis, Bull. New York Acad. Med. **19**:301-316, 1943.

In a series of 129 verified cases Bollack, David and Puech [17] noted the following distribution of field defects:

| | Percentage |
|---|---|
| Central scotoma | 31 |
| Concentric contraction | 23 |
| Bitemporal hemianopsia | 17 |
| Binasal depression | 7 |
| Lateral homonymous hemianopsia | 5 |
| Altitudinal hemianopsia | 5 |

In 12 per cent of the cases the fields were normal, they were not mentioned, they could not be charted on account of poor vision or they were so irregular that the authors were unable to classify them.

Deery [9] mentioned central scotoma in 4 of his 13 cases, and Craig and Lillie,[13] in 4 of their 8 cases. Central scotoma is therefore an essential feature. It is bilateral, usually very large and can be found together with a peripheral contraction of the field.

Concentric contraction was observed by Heuer and Vail [11] in 3 of their 4 cases, by Morea [15b] in 3 of 9 cases and by di Marzio and his co-workers [15c] in 3 of 7 cases. The field is irregularly depressed and sometimes notably contracted. Sometimes a central scotoma is present. In some cases this irregular contraction predominates on one side, and the field is then classified as one of the following types:

1. Bitemporal field defects are often irregular, and concentric depression of the field is more pronounced on the temporal side. The fields are almost never as regular as with adenoma of the pituitary or a suprasellar meningioma, and the changes do not follow the usual progression, from the temporal superior to the temporal inferior quadrant and then to the nasal inferior and the nasal superior quadrant. A central scotoma is also often present, even at an early stage.

2. A few cases of binasal depression have been reported in association with optochiasmic arachnoiditis and Vincent and I observed 4 instances of this rather unusual field defect.[33] Craig and Lillie [13] expressed the belief that it was related to a fairly anterior pressure, exerted on the optic nerves rather than on the chiasm.

3. Lateral homonymous hemianopsia, when present, is sometimes complete, and sometimes of only quadrant type. The field defects are usually atypical and incongruous. Craig and Lillie [13] observed an unusually large proportion of cases in which they were present: 3 out of 8 cases. Deery [9] noted them in 2 of 13 cases of this form of arachnoiditis. A few more cases have also been reported.

4. Di Marzio, Cavina and di Negris [15c] observed 4 cases of altitudinal hemianopsia in their series of 7 cases of optochiasmic arachnoiditis, the condition being inferior in 3 cases and superior in 1 case. I have personally observed 1 case of the inferior type, due to pressure of the anterior cerebral artery on the superior aspect of the chaism.[30]

*Visual Acuity.*—Contrary to what usually occurs in cases of pituitary adenoma, the visual acuity fails at an early stage of the disease. This loss of vision is bilateral in most cases, but some cases of unilateral loss have been reported. When it is bilateral, one eye is often affected before the other. Visual acuity may fail slowly, as in cases of perichiasmic tumors, but the loss of vision is sometimes rapid, or even sudden: occurring in two weeks in 2 cases of Heuer and Vail,[11] in one month in a case of di Marzio, Cavina and di Negris [15c] and in three months in a case of Cossa.[34] Craig and Lillie [13] concluded that rapid failure of vision was characteristic of this disease.

*Fundus.*—The disk is rarely normal, at least at the stage at which the patient is usually examined. In a series of 129 verified cases, Bollack, David and Puech [17] noted the following distribution of changes:

| | Percentage |
|---|---|
| Primary optic nerve atrophy | 38 |
| Optic nerve atrophy with blurred margins | 16 |
| Papilledema | 10 |
| Temporal discoloration | 7 |
| Hyperemia of the disk | 7 |
| Altitudinal atrophy | 4 |
| Normal disk | 10 |
| Unclassified | 8 |

Di Marzio, Cavina and di Negris [15c] noted atrophy either of the lower or of the upper half of the disk. The other half of the disk showed slight edema, and in all the cases altitudinal hemianopsia was present. Vail [22] asserted that the appearance of an atrophy which lies between the primary and the secondary type of atrophy was highly suggestive of arachnoiditis, and such has been my own experience.

*Other Symptoms.*—Symptoms other than visual disturbances are unexpectedly rare. A few, but only a few, cases have been reported in which oculomotor or abducens paralysis,

33. Vincent, C., and Hartmann, E.: Douze observations de rétrécissement binasal du champ visuel au cours d'affections intracraniennes, Ann. d'ocul. **171**:193-207, 1934.

34. Cossa, P.: Cécité par névrite optique, intervention sur la region opto-chisamatique, Rev. d'oto-neuro-opht. **11**:441-444, 1933.

nystagmus, trigeminal anesthesia and pupillary inequality were present, their scarcity showing how localized the arachnoiditis usually is.

Headache is more frequent and is noted in about one third of all cases. The pain is usually frontal; in other cases it is localized behind the eyes, and it often radiates to the neck and shoulder. This is an early symptom and often appears before there are any visual disturbances. Drowsiness is sometimes also present, with moderate elevation of temperature, nausea and dizziness. These symptoms are usually temporary and may have disappeared when vision fails and the patient is first examined.

Few patients have other neurologic symptoms, such as anosmia, facial paralysis, auditory and vestibular disturbances, polydipsia, polyuria, obesity and dyspituitarism.

The spinal fluid is usually normal. In a few patients there was a moderate increase in the protein content or of the cell count.

*Roentgenographic Evidence.*—Roentgenologic studies are helpful in that they show none of the signs usually found with sellar or suprasellar tumors. The sella is not enlarged, as with adenoma of the pituitary. In exceptional cases an infrachiasmic pocket of serous meningitis may give the picture usually observed in cases of glioma of the optic chiasm or of the optic nerves. Puech [35] reported such a case in which both optic foramens were enlarged and in profile the sella was Ω shaped. Ryan [36] observed destruction of the bone in the posterior wall of the optic canal on one side. Calcareous deposits have been observed in exceptional cases (François [26]). Opacity of the sinuses is frequently noted, and in some cases a shadow extends to the base of the skull in the middle fossa. Hirtz and Worms [37] stressed the value of this sign in cases of "perisinusitis."

Air studies usually prove the ventricles to be of normal size and location; in some cases they are even reduced in size (Vincent, David and Puech [38]). Encephalography was found useful by Lillie [39]: The chiasmic cistern is irregular and deformed. Compensatory channels are apparent in the frontal and occipital poles, and there is interference at the vertex with the normal pathways of the subarachnoid fluid. Slight cortical atrophy is suggested. The essential feature is the absence of evidence of a space-taking lesion within the cranium. Fay [40] noted that stereoscopic encephalograms sometimes revealed adhesions in the chiasmic region.

35. Puech, P., in Bollack, David and Puech,[17] pp. 49 and 130.

36. Ryan, E. R.: Optochiasmatic Arachnoiditis, Arch. Ophth. **29**:818-825 (May) 1943.

37. Hirtz, E. J., and Worms, G.: Des "périsinusites" profondes; leur image radiologique, Ann. d. mal. de l'oreille **45**:833 (Sept.) 1926.

38. Vincent, C.; David, M., and Puech, P.: Sur la ventriculographie, Rev. neurol. **40**:1031-1096, 1933.

39. Lillie, W. I.: Prechiasmal Syndrome Produced by Chronic Local Arachnoiditis, Arch. Ophth. **24**:940-947 (Nov.) 1940.

### DIAGNOSIS

From the preceding discussion one realizes that optochiasmic arachnoiditis is polymorphous and that the diagnosis cannot be approached in the same way in all cases.

In some cases the temporal field defects suggest pressure on the chiasm, and therefore the presence of a sellar or a suprasellar tumor. But with arachnoiditis the bitemporal depression is usually not exactly the same as with such tumors: It is less regular both in pattern and in growth. In most cases a more or less concentric contraction predominates on the temporal side of each field. With intrasellar tumors (adenoma of the pituitary and intrasellar craniopharyngioma) there are more symptoms of dyspituitarism, and the sella appears enlarged in a profile roentgenogram. A suprasellar tumor, such as a meningioma of the tuberculum sellae or a meningioma lying in the very posterior part of the olfactory groove should also be considered; however, such a tumor usually comes into view in air ventriculograms, and in some cases the tuberculum sellae gives an abnormal picture both in the anteroposterior and in the lateral roentgenogram. Suprasellar craniopharyngioma is often detected by a roentgenogram or an air encephalogram and is usually more noticeably associated with symptoms of hypothalamic and infundibular involvement. The tumor also occurs at an earlier age. Glioma of the chiasm may offer difficulty in differential diagnosis, since the field defects are fairly similar and pockets of serous meningitis may sometimes give a roentgenographic picture somewhat like that of glioma. Fortunately, gliomas are met mostly in children, who rarely have arachnoiditis. Moreover, other symptoms of Recklinghausen's disease are sometimes present and are then helpful. Bitemporal field defects may also accompany nontumoral diseases, such as multiple sclerosis, encephalitis and Roenne's [41] chiasmic form of retrobulbar neuritis, but with these diseases the visual disturbances are more often of a different type, as I shall indicate later.

The diagnosis is approached differently if the patient has bilateral optic nerve atrophy with a

40. Fay, T., in discussion on Lillie.[39]

41. Roenne, H.: Ueber akute Retrobulbärneuritis im Chiasma lokalisiert, Klin. Monatsbl. f. Augenh. **55**:68-97, 1915; On Nonhypophyseal Affections of the Chiasma, Acta ophth. **6**:332-343, 1928.

concentric and more or less regular contraction of the field. A few features are at once suggestive of arachnoiditis: bilateral involvement of the eyes, the presence sometimes of a central scotoma and frequent slight edema superimposed on the primary optic nerve atrophy. In most cases infectious optic neuritis does not produce a similar picture; in very few cases is this condition bilateral. Syphilis is more likely to be considered in the form either of chronic syphilitic meningitis or of tabes. The diagnosis of the former condition is not always easy, or even possible, since syphilis may in some cases be the cause of arachnoiditis. It is a moot point to decide how frequently syphilis is an etiologic factor and whether and when surgical intervention is advisable. The optic nerve atrophy of tabes is more easily diagnosed, but some authors have questioned whether operation might not sometimes be helpful in cases of this condition. I had an operation performed in a case of this type; although the patient had tabes, a rapidly failing vision and altitudinal hemianopsia made me wonder whether there was not an arachnoid stricture which could be removed. I have already referred to this case. The point is not to make a diagnosis of arachnoiditis from chronic syphilitic meningitis and from tabes, but rather to determine in which cases tabes and meningitis may benefit from surgical treatment. Such cases are rare, but more may be learned about them in the future. In syphilitic patients treated with pentavalent arsenic bilateral toxic neuritis with peripheral contraction of the fields must occasionally be considered.

It is in cases of the type with bilateral central scotoma that diagnosis is the least easy. Toxic amblyopia, with bilateral central defects due to intoxication with such substances as alcohol, tobacco, lead, thyroid and carbon disulfide, is usually readily recognizable from the history. Moreover, the central scotoma of arachnoiditis is larger and irregular in shape, and there is often a peripheral contraction. Most infectious optic neuritis is unilateral, whether due to syphilis, sinus disease or other focal infection. It is only when both optic nerves are affected that one considers arachnoiditis. Here, again, when a sinus infection or syphilis causes a bilateral central scotoma it is not easy to differentiate the two conditions, since both diseases can cause arachnoiditis, and one is usually more concerned with the advisability of a chiasmic exploration than with a purely academic diagnosis. Multiple sclerosis, Devic's disease (optic neuroencephalomyelopathy) and disseminated encephalitis, especially the first two conditions, are more likely to affect both optic nerves. The diagnosis is difficult when the visual symptoms appear before all others. Such is sometimes the case with multiple sclerosis, but the optic neuritis is then usually acute or subacute, in contrast to the chronic course of arachnoiditis. It is only in the less frequent cases in which bilateral slowly progressive optic nerve atrophy appears as an initial symptom of multiple sclerosis that the diagnosis is difficult. Roenne's chiasmic retrobulbar neuritis is not universally accepted and is rare in any case. Spinal symptoms are often present; the evolution is subacute, and field defects are changeable. It is possible that a majority of cases of this condition would now be classified with the demyelinating diseases and that in some instances arachnoiditis may have been present. Leber's disease (hereditary optic atrophy) should be easily recognized, with its history of familial optic nerve atrophy. It should be noted, however, that in some cases of this disease operations revealed optochiasmic arachnoiditis. Davis and Haven [19] reported such a case, and Vincent and his associates have operated in 4 other instances.[17] Such facts are disturbing.

### TREATMENT

If any possible cause is found, such as sinus infection, syphilis or rheumatic fever, therapeutic measures are self evident. They should not be continued, however, without discretion, and if the arachnoiditis does not respond within a reasonable time and the visual disturbances continue to increase, operation should be considered.

Even if no evident etiologic factor is found, nonoperative treatment is advisable within normal time limits. Several forms of medication, such as intravenous injections of sodium salicylate, sodium iodide, mercuric cyanide, methenamine and thiamine chloride, use of neurotropic vaccines and nonspecific protein therapy, have been advocated, but none has proved effective. Semipenetrating roentgen radiation should also be applied, and this treatment can be employed while some of the preceding forms of medication are being tried. If there is no improvement, especially if vision continues to fail and the field becomes more defective, surgical intervention should not be delayed too long.

The chiasmic region can now be explored with but slight mortality, and one is entitled to take some risks if all other procedures have failed and blindness is to be feared. In 1936 Vincent, Puech and Berdet [14c] reported on a series of 95 operations, with 7 deaths. Three of the deaths

occurred among the first patients to be operated on, and the technic was eventually improved. Of the other 4 patients, 1 was aged and died of bronchopneumonia a few days after the operation.

The visual results are far from being as favorable as those which follow removal of a tumor. Statistics vary considerably, which is to be expected, as the series are short and most of the reports are incomplete. The largest complete series is that from the Pitié Hospital, in Paris, reported by Bollack, David and Puech.[17] Of these 66 cases, improvement occurred in 19 (28 per cent) and the result of the operation was doubtful or poor in the other 47 cases. Of the 63 cases previously reported by several neurosurgeons and collected by Bollack, David and Puech, improvement occurred in 29 (46 per cent). It is difficult to know whether the notable difference between the two figures is due to the fact that most of the previously reported cases were the favorable ones, to a difference in surgical technics, or to the willingness of Vincent and his co-workers, at the Pitié Hospital, to attempt surgical treatment even in the most hopeless cases.

It is not clear at present whether the cystic or the adhesive type carries the best prognosis for visual improvement. Strangely, the appearance of the optic nerves is not a sure guide, except, of course, in cases of extreme atrophy. There is, unfortunately, no standard by which one can form any judgment, before operation, of which patients should be operated on and may improve and which will not respond to surgical treatment. Even conditions of long standing have improved to a certain extent, but on the whole results have been far better when operation was done in the early stages of the disease.

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## Correspondence

### PARESIS OF RIGHT SUPERIOR OBLIQUE AND OF LEFT SUPERIOR RECTUS MUSCLE: DIFFERENTIAL DIAGNOSIS

*To the Editor:*—In January 1938 Dr. Alfred Bielschowsky, then director of the Dartmouth Eye Institute, delivered ten lectures before the Los Angeles Research Study Club on motor anomalies of the eyes. The eighth and ninth lectures had previously been published in this journal (Lectures on Motor Anomalies of the Eyes: II. Paralysis of Individual Eye Muscles, ARCH. OPHTH. **13:** 33 [Jan.]; IV. Functional Neuroses: Etiology, Prognosis and Treatment of Ocular Paralysis, ibid. **13:** 751 [May] 1935). Most of this material is republished in the November 1944 issue of the ARCHIVES, page 372, as the text for a paper by Dr. William Thornwall Davis, entitled "Paresis of Right Superior Oblique and of Left Superior Rectus Muscle: Differential Diagnosis."

In this country ophthalmologists with few exceptions have accepted the views of Dr. Alexander Duane concerning the differential diagnosis of vertical motor anomalies. His opinions have been popularized by Dr. James W. White, at the New York Post-Graduate Medical School and Hospital, where I have been on the faculty for twenty-five years. Since the publication of Bielschowsky's lectures two years ago, my colleagues and I have observed that ophthalmologists from the West Coast in our eye muscle courses feel strongly with Bielschowsky that "by far the most frequent and important type of paralysis of a simple vertical motor anomaly is trochlear nerve palsy." Dr. Davis reports that "of 88 cases of paresis of the superior oblique and the superior rectus muscle, the superior oblique was involved in 48, or 54.5 per cent, and the superior rectus in 40, or 45.5 per cent." In sharp contrast are the results of an exhaustive clinical study of 527 cases by Dr. J. W. White and Dr. Harold W. Brown (Occurrence of Vertical Anomalies Associated with Convergent and Divergent Anomalies, ARCH. OPHTH. **21:** 999 [June] 1939), with the superior oblique muscle involved in 20 cases, or 4 per cent, and the superior rectus muscle in 507 cases, or 96 per cent. It is not possible that these authorities overlooked about 50 per cent of their cases with involvement of the superior oblique.

Publication of Dr. Davis' paper once more revives the dormant Bielschowsky-Duane argument and, unfortunately, will create confusion in the minds of the younger ophthalmologists. Although Dr. White remarked in his discussion on Dr. Davis' paper (page 379) that "in 1914, . . . Bielschowsky never convinced Duane; . . . Duane never convinced Bielschowsky, [and] Dr. Davis has not convinced me," I trust that the brilliant and lasting contributions of Bielschowsky will never again be clouded by conflicting opinions on one small aspect of his voluminous research.

In the hope that this time-worn controversy will be settled, I suggest that the Section on Ophthalmology of the American Medical Association, at its Philadelphia meeting in June 1945, appoint a committee to standardize the differential diagnosis of paralysis of the superior oblique and of the superior rectus muscle.

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# Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

## Conjunctiva

INCLUSION BLENNORRHEA. J. H. ALLEN, Am. J. Ophth. **27:** 833 (Aug.) 1944.

Allen divides this article into two sections, the first giving the data on 43 cases of inclusion blennorrhea with respect to incidence, seasonal variation, cause and manifestations. In the second section he found that, contrary to Lindner's suggestion, in a series of 43 consecutive conjunctival passages the etiologic agent of inclusion blennorrhea did not change its disease-producing characteristics or progressively alter its virulence.

W. S. REESE.

UNILATERAL MEMBRANEOUS CONJUNCTIVITIS WITH COMPLETE CAST. J. F. GALPINE and D. R. CAMPBELL, Brit. J. Ophth. **28:** 412 (Aug.) 1944.

In a girl aged 6 years the ocular condition developed during an attack of scarlet fever, complicated by vulvovaginitis. Smear of material from the eye showed a large number of gram-negative diplococci, both intracellular and extracellular, which were indistinguishable from gonococci. The latter were never obtained in culture. The appearance was that of membranous conjunctivitis. The report on the culture indicated that the infection was streptococcic. In its development the membrane almost hid the cornea and extended from the limbus as a complete lining throughout the conjunctival sac. About one month from the onset the membrane came away as a complete cast.

W. ZENTMAYER.

LYMPHOCYTOSIS AND ITS SIGNIFICANCE IN EYE DISEASES. S. V. OAK, Indian J. Ophth. **4:** 78 (Oct.) 1943.

Oak discusses the origin of lymphocytes and points out that they play an important part in chronic inflammatory processes of the eye. He gives a clinical description of the conjunctival conditions of which they are an important histologic feature.

## Congenital Anomalies

CONGENITAL FOLDS OF THE RETINA. A. VAZQUEZ BARRIERE and L. A. BOADO, Arch. de oftal. de Buenos Aires **18:** 572 (Nov.) 1943.

This malformation consists in a crease of the retina, forming a fold above the retinal plane, always beginning at the papilla and spreading toward the periphery in fan fashion. Frequently the peripheral end extends beyond the limits of the ophthalmoscopic field, reaching the ciliary body, and even the equator of the crystalline lens.

Only four important papers on this condition have appeared thus far, and up to the time of writing only 40 cases have been reported in the literature.

The authors describe 2 cases illustrating this rare condition.

H. F. CARRASQUILLO.

## Cornea and Sclera

INFRA-RED THERAPY OF FLASH KERATOCONJUNCTIVITIS. D. G. COGAN, V. E. KINSEY and P. DRINKER, J. A. M. A. **123:** 883 (Dec. 4) 1943.

The authors supply the following summary: "Keratoconjunctivitis was produced in rabbits by exposure to a mercury vapor arc. After the establishment of doses that would result in reproducible signs, alternate eyes were treated by means of a therapeutic heat lamp. No evidence was obtained to indicate that this form of treatment benefited the keratoconjunctivitis."

W. ZENTMAYER.

PARENCHYMATOUS KERATITIS IN A CASE OF ACQUIRED SYPHILIS. TARIK OZERENGIN, Göz. klin. **1:** 52, 1943.

The author describes a case of parenchymatous keratitis with iritis in a woman aged 40 with syphilis who was observed over a period of seven years. The author concludes that keratitis with gumma of the legs existed and that, contrary to the general belief, the corneal disease may occur not only as a secondary, but as a tertiary, lesion. Treatment with mercury and arsenic brought about rapid improvement, but not without further relapses.

W. ZENTMAYER.

## General

VITAMIN P IN OPHTHALMOLOGY. W. R. MATHEWSON, Brit. J. Ophth. **28:** 336 (July) 1944.

In 2 cases of ocular hemorrhage vitamin P was used, with satisfactory results: In the first case the patient had extensive retinal hemorrhages and hemorrhages of the nose and bladder, but on administration of vitamin P the nasal and vesical hemorrhages ceased, no fresh retinal hemorrhages occurred and those present were absorbed. The

patient had myelomas, and the nasal hemorrhage was characterized by large clots of blood and serum.

In the second case the patient had recurrent hemorrhage into the anterior chamber after extraction of a cataract; but after administration of vitamin P there was no recurrence, and the iris, which had become muddy, rapidly cleared. The eye, which was looking unhealthy, rapidly took on a healthy tone. The patient improved greatly and rapidly in general appearance and mental agility when vitamin P was given.

In conclusion, it is suggested that there is a case calling for investigation of vitamin P because, so far as can be judged from the evidence in these 2 cases, vitamin P is of value in ophthalmology.

W. ZENTMAYER.

## General Diseases

MIKULICZ DISEASE [HYPERTROPHY OF THE SALIVARY AND LACRIMAL GLANDS]. M. VILLANUEVA and C. S. DAMEL, Arch. de oftal. de Buenos Aires **18**: 559 (Nov.) 1943.

The author reports a typical case of the disease in a man aged 33. The patient had a history of a primary syphilitic lesion and a positive Wassermann reaction of the blood, for which he had received treatment.

The sublingual and parotid glands on the left side were enlarged and tender. The left eye showed some protrusion of the globe, edema of the lids and congestion of the conjunctiva. Treatment was with calcium, iodine, arsenic, antisyphilitic drugs and roentgen ray therapy, with no encouraging results.

A brief discussion of the syndrome is given. Photographs of the patient appear in the article.

H. F. CARRASQUILLO.

## Glaucoma

THE USE OF DORYL [CARBAMINOYLCHOLINE CHLORIDE] IN GLAUCOMA. J. F. HARDESTY, Am. J. Ophth. **27**: 625 (June) 1944.

Hardesty concludes that carbaminoylcholine chloride is not effective in all cases of glaucoma, and is even contraindicated in some instances, but that from his experience in other cases, as well as in the 9 cited, the drug is a valuable adjuvant in the treatment of glaucoma.

W. S. REESE.

SURGICAL CONTROL OF GLAUCOMA IN THE NEGRO. C. E. ILIFF, Am. J. Ophth. **27**: 731 (July) 1944.

Iliff reaches the following conclusions:

"1. Primary glaucoma in the Negro was controlled in 54.2 per cent of the cases by the filtering operation.

"Secondary glaucoma was controlled in only 44 per cent of the cases by the filtering operation.

"2. Iridencleisis is superior to trephining as an initial operative procedure and the complications are less severe.

"3. Trephining or cyclodialysis is the operation of choice as a second operative procedure after one operative failure.

"4. When operative failure occurred, it was noted within the first six months in over 85 per cent of the cases.

"5. Postoperative beta irradiation of the blebs in filtering operations give encouraging results and is worthy of further trial."

W. S. REESE.

## Hygiene, Sociology, Education and History

VISUAL PHYSIOLOGY OF THE CINEMA. GEORGE H. BELL, Brit. M. J. **2**: 669 (Nov. 27) 1943.

At the Tennent Institute of Ophthalmology, Western Infirmary, Glasgow, Scotland, Dr. George H. Bell, from the Institute of Physiology, of the University of Glasgow, delivered a lecture on the subject indicated in the title. He anticipates a great exploitation of the moving picture as a teaching medium and therefore thinks it important that medical people should have some elementary knowledge of the physiologic problems concerned with moving pictures. For educational purposes, a 16 mm. equipment is regarded as satisfactory. The details of the picture can be clearly seen if the observer is seated not more than 6 screen widths from the screen. Those who are seated nearer find that the picture lacks sharpness and that the accommodation is apt to tire, and they experience flicker and other symptoms of fatigue. The screen with the usual 2 inch (5 cm.) lens should be 5½ screen widths from the screen. The best position to get a perspective of the projected pictures is halfway back. It is also important not to sit too much to the side. For school projection the viewing angle should not be more than 30 degrees. The committee recommended (*a*) that a picture width equal to one-sixth the distance from the farthest row of seats to the screen position should be adopted for classroom projection; (*b*) that no pupil should be seated closer to the screen than twice the picture width, and (*c*) that no row of seats should be longer than its distance from the screen. The screen with a mat surface is 90 per cent as bright at an angle of 30 degrees as when viewed directly from the front, while a screen coated with small glass beads is four times as bright, but the maximum viewing angle is narrowed to 20 degrees. For a square room the mat screen is the best, and the coated type may be used in a long room. The brightness of the projected picture should be 10 foot lamberts with the projector running, but with no film in the machine. The efficiency is lost if the light is

too weak or if it is too strong. The quality of the picture suffers, also, if the projection room is not adequately darkened.

The author concludes with comments on the illusion of reality and states that even when stereoscopy is added, many things will still be missing for complete illusion.

ARNOLD KNAPP.

## Ocular Muscles

OPHTHALMOPLEGIA AND RETINAL DEGENERATION. R. I. BARNARD and R. O. SCHOLZ, Am. J. Ophth. **27:** 621 (June) 1944.

Barnard and Scholz give the following summary:

"Four cases of various types of retinal degeneration with complicating ophthalmoplegia are reported. Although other factors were present which might account for the ophthalmoplegia, it was felt that the association is more than a coincidence. It is suggested that the two constant features in these cases, ophthalmoplegia and retinal degeneration, with secondary pigmentary changes, may be a syndrome due to some common etiologic factor."

W. S. REESE.

CORRECTION OF EXTERNAL-RECTUS PARALYSIS WITH CONTRACTURE OF THE OPPOSING INTERNUS. P. H. REINHARDT, Am. J. Ophth. **27:** 636 (June) 1944.

Reinhardt states that transplantation operations offer a cosmetic and functional cure for paralyses of the external rectus muscle which do not clear up and that operation should be performed before contracture of the internal rectus muscle occurs.

W. S. REESE.

## Parasites

ORBITAL MYIASIS. L. A. BARRIERE, Arch. de oftal. de Buenos Aires **18:** 585 (Nov.) 1943.

The author discusses the rare condition of ophthalmomyiasis and reports a case in which it involved the orbit. The disease was present in an inmate of an insane asylum. An extensive ulceration took place in the right orbit, which destroyed the lower lid and extended almost to the apex of the orbit. The first two phalanges of the index and middle fingers could be placed in the opening. Larvae were encountered at the base of the ulceration in great numbers. According to the parasitologic report, these larvae belonged to the genus Chrysomyia, species Cochliomyia hominivorax, the fly which produces myiasis in animals. Owing to the extension of the ulcerative process, the eyeball was wholly destroyed. The condition was treated by removal of the larvae (153 of which were found) and daily intravenous injections of mercuric oxycyanide. The patient was cured.

H. F. CARRASQUILLO.

## Physiology

THE SECRETION-DIFFUSION THEORY OF INTRAOCULAR FLUID DYNAMICS. V. E. KINSEY and W. M. GRANT, Brit. J. Ophth. 28: 355 (July) 1944.

From comments on the authors' recent article (The Mechanism of Aqueous Humour Formation Inferred from Chemical Studies on Blood-Aqueous Humour Dynamics, *J. Gen. Physiol.* **26:** 131 [Nov.] 1942) Kinsey and Grant feel that recapitulation of their theory of intraocular dynamics is in order. They summarize their present concept of aqueous humor dynamics by stating their belief that the electrolytes enter the anterior chamber as a result of secretion and the nonelectrolytes by diffusion. Both electrolytes and nonelectrolytes, they believe, leave the anterior chamber by a process of flow. The authors then discuss the criticism made by Duke-Elder and Davson of their statement of the mechanism of ultrafiltration and outflow.

W. ZENTMAYER.

## Retina and Optic Nerve

A TYPE OF FOVEO-MACULAR RETINITIS OBSERVED IN THE U. S. NAVY. F. C. CORDES, Am. J. Ophth. **27:** 803 (Aug.) 1944.

Cordes describes an unusual type of foveomacular retinitis seen in Navy personnel in the Hawaiian and South Pacific areas. The lesion is limited primarily to the fovea and starts with macular edema. Later the picture is that of a hole or cyst in the fovea surrounded by a gray area. This may eventuate in a honeycombed condition. Treatment seems ineffective, and the etiologic agent has not been determined.

W. S. REESE.

ALMOST COMPLETE RETINAL DETACHMENT AFTER CATARACT EXTRACTION; COMPLETE REATTACHMENT AFTER GLAUCOMA ATTACK. F. NELSON, Am. J. Ophth. **27:** 876 (Aug.) 1944.

Nelson reports a case of total detachment of the retina in a man aged 80 following intracapsular extraction of a hypermature cataract. The detachment persisted for several months, during which the eye was practically blind. Complete reattachment and full restoration of function then occurred, after an acute glaucomatous attack.

W. S. REESE.

EMBOLISM OF A BRANCH OF THE CENTRAL ARTERY OF THE RETINA WITH CURE: REPORT OF TWO CASES. P. SATANOWSKY, Arch. de oftal. de Buenos Aires **18:** 579 (Nov.) 1943.

Alterations in the endothelium of the left side of the heart or the aorta may produce a coagu-

lum which may give rise to an embolus. The walls of the artery at the level in which the embolus is lodged react, and embolic arteritis results. The changes in the territory supplied by the vessel depend on the terminal character of the artery or the existence of insufficient anastomotic branches. When the embolus is small and has been retained by a reactive spasm of the vessel, it may migrate to a smaller branch on relaxation of the spasm through treatment; the visual disturbances may then be much reduced or may disappear altogether if the embolus is washed out by the blood current.

The author describes 2 cases in which such results were obtained after treatment with the antispasmodic drugs acetylcholine and nicotinic acid.

H. F. CARRASQUILLO.

### Toxic Amblyopia

THE ETIOLOGY AND TREATMENT OF TOBACCO-ALCOHOL AMBLYOPIA. F. D. CARROLL, Am. J. Ophth. **27:** 712 (July); 847 (Aug.) 1944.

Carroll gives this summary and draws the following conclusions:

"Approximately 175 patients with tobacco-alcohol amblyopia have been observed by the writer in the nine-year period 1933-1942. In the last seven years 25 of these patients have been allowed to maintain their usual intake of alcohol and tobacco under the following conditions:

"An initial group of 11 patients was placed on a diet adequate in all respects and supplemented with brewers' yeast.

"A second group of five patients was left on its usual diet and given vitamin-B complex.

"A third group of four hospitalized patients was placed on a diet inadequate in all known vitamins and given large amounts of vitamin-B complex.

"A fourth group of five hospitalized patients was placed on the same inadequate diet and given synthetic vitamin $B_1$ only.

"All the patients on these various regimes made partial or complete recoveries in spite of their continued and unabated use of alcohol and/or tobacco. The vision in 21 patients was 20/30 O. U. or better after treatment and in 14 was 20/20 or better. These results were at least as good as those obtained by the author in any previous consecutive 25 patients with this condition, including those who abstained from the use of tobacco and alcohol while under treatment.

"The fact that all of the patients in the fourth group improved and one made a complete recovery is of special significance since in this group every known factor other than vitamin $B_1$ which might have caused improvement had been eliminated. In spite of this result, however, it is recommended that the whole vitamin-B complex be administered as well as thiamin alone in the treatment of these cases."

The most likely explanation of tobacco amblyopia at this time is that it is the result of a "toxic" action of tobacco on malnourished cells. When thiamine is added, the nutrition of the damaged cells, or perhaps their axons, improves, and the injurious agent is no longer injurious. It seems likely from present evidence that in persons consuming, absorbing and utilizing normal amounts of vitamin B tobacco amblyopia does not develop.

W. ZENTMAYER.

## CORRECTIONS

In the article by Dr. Carlos Weskamp entitled "Bowen's Disease of the Coronea," in the April issue (ARCH. OPHTH. **31:** 310, 1944), "osteitis deformans" was erroneously inserted in line 3 of the fourth paragraph. The term Paget's disease refers here to the cutaneous disease of the nipple.

In the abstract of a paper by Dr. William F. Hughes entitled "Chemical Burns of the Eye," in the November 1944 issue of the ARCHIVES, "or a 0.05 molar solution," on line 9 of the paragraph on "Alkali Burns," should read "and a 0.05 molar solution."

# Society Transactions

EDITED BY DR. W. L. BENEDICT

## NEW YORK ACADEMY OF MEDICINE, SECTION ON OPHTHALMOLOGY

FRANK C. KEIL, M.D., *Chairman*

WILLIS S. KNIGHTON, M.D., *Secretary*.

*May 15, 1944*

**End Results of Intraocular Foreign Bodies.** DR. FREDERICK H. HULL, Passed Assistant Surgeon, United States Public Health Service (by invitation).

The end results obtained in any given case of intraocular foreign body depend largely on the amount of damage done to the structures of the eye as the foreign body travels through the globe. Hemorrhage in the vitreous of any extent is usually serious, and the development of infection, particularly panophthalmitis, is disastrous.

At the Marine hospital with which I am associated the practice is to attempt removal with the hand magnet through the wound of entrance, with the use of local anesthesia and retrobulbar injection of procaine, when the foreign body is in the iris or the anterior chamber. The corneal wound is then covered with a conjunctival flap. If the wound of entrance has healed, the foreign body is removed through a keratome incision.

When the foreign body has been localized in the vitreous chamber, my associates and I have employed both the anterior and the posterior route. With the first approach, the giant or the hand magnet is used to bring the foreign body to the posterior capsule of the lens, through the zonule and then into the anterior chamber, from whence it can be removed through a keratome opening. When removal is attempted by the posterior route, the scleral site nearest the foreign body is laid bare and the foreign body removed by means of the hand magnet through a radial sclerotomy opening. Diathermy punctures are placed routinely about the scleral incision. The posterior approach has given better results than the anterior approach. All patients receive either a prophylactic dose of tetanus antitoxin or a "booster dose" of tetanus toxoid. Oral administration of sulfathiazole and sulfadiazine has not seemed to lessen the incidence of infection.

In a series of 24 consecutive cases encountered prior to 1943, the foreign body was in the anterior chamber in 37 per cent and in the posterior chamber in 63 per cent. Of the cases in which the body was in the anterior chamber, good vision was retained in 55 per cent; cataract developed in 22 per cent, and enucleation was necessary in 11 per cent. Of the cases in which the foreign body occurred in the posterior chamber, useful vision was retained in only 27 per cent; cataract developed in 27 per cent; a hemorrhage in the vitreous large enough to cause serious visual loss occurred in 13 per cent, and the process went on to enucleation in 33 per cent.

The following cases are reported as clinical examples of some of the results obtained, both good and bad.

REPORT OF CASES

CASE 1.—A carpenter's mate aged 26 felt something hit his left eye while clawing a nail from a piece of wood. The next day vision was 14/21 in the right eye and 14/89 in the left eye. There was a laceration of the cornea 2 mm. long at 9 o'clock on the limbus. A metallic foreign body beneath this impinged on the iris at 10 o'clock. The foreign body was removed with the hand magnet through the wound of entrance on the day of examination. Convalescence was uneventful except for a moderate amount of iritis. The tension has remained normal for two months, and vision is 20/20 —1 in each eye.

CASE 2.—A machinist aged 45 put his glasses on his forehead, and a chip from the hammer of a fellow-worker, 3 or 4 feet (90 or 120 cm.) away, struck his right eye, producing a penetrating wound of the cornea directly below the pupil. The anterior chamber was cloudy and the iris was pulled downward. Roentgenographic examination revealed a foreign body 8 by 2 by 1.5 mm., situated in the vitreous chamber. With the hand magnet, the foreign body was extracted through the wound of entrance. The progress was steadily downhill. The lens became cataractous. The eye was severely inflamed, and vision was completely lost. The tension was below normal. Two months later the right eye was enucleated, with the patient under anesthesia induced by intravenous injection of sodium pentothal. Convalescence from this operation was uneventful.

CASE 3.—A shipfitter aged 49 felt something hit his left eye when drillers drilled through from the other side of a bulkhead on which he was hammering. Vision was 20/30 in the right eye and was limited to hand movements in the left eye. A penetrating wound of the sclera, 2 mm. long, lay 3 mm. behind the limbus, at 4 o'clock. The cornea, the anterior chamber and the lens were clear, but the vitreous was filled with blood. Roentgenographic examination and localization by the Sweet method revealed an intraocular foreign body, 2.5 by 2 by 2 mm., situated 10 mm. below the horizontal plane, 2 mm. nasal to the vertical plane and 7 mm. behind the cornea. Operation was performed on the day of admission, the hand magnet being used to bring the foreign body through the zonule and into the anterior chamber, from which it was removed through a keratome incision. The foreign body on withdrawal became enmeshed in the iris, a small portion of which prolapsed. This portion was excised. The keratome section healed normally, but the scleral wound did not close completely; so a conjunctival flap was placed

over the wound. Subsequently the scleral wound healed normally. Six weeks after the accident a traumatic cataract began to develop. The tension has remained normal for seven months, but the cataract has become increasingly dense. Vision was 20/20 with correction in the right eye and was limited to light perception in the left eye.

CASE 4.—A laborer aged 38 felt something hit his right eye while cutting a piece of tin with a hammer and chisel. He was treated at another hospital for two weeks before I saw him.

At that time vision was corrected to 20/20 in each eye. No wound of entrance was noted in the cornea or the sclera. The vitreous was fluid, and a few floaters were present. Roentgenographic localization by the Sweet method revealed a foreign body 6 mm. below the horizontal plane, 5 mm. temporal to the vertical plane and 16 mm. behind the cornea. One week later the foreign body was withdrawn posteriorly by the hand magnet through an L-shaped scleral incision. Diathermy punctures were placed about the sclerotomy opening, and the conjunctiva was closed. Convalescence was uneventful. Vision in each eye remained 20/20 with correction.

Four years after the accident the patient complained of blurred vision in the right eye. There was no pain. No previous attacks had been noted. Vision was corrected to 20/25 in each eye. The cornea of the right eye was hazy. The disk was indistinct, but no increased cupping was seen. Tension was 60 mm. (Schiøtz) in the right eye and was normal in the left eye. The patient was confined to bed, and 1 drop of a 1 per cent solution of pilocarpine nitrate was instilled every two hours in the right eye. The tension decreased promptly to normal and has remained so. He has returned for observation every two months since that time, and the fields and fundi remain normal.

DISCUSSION

DR. CONRAD BERENS: Dr. Hull's report is most interesting to me, especially because of his preference for the posterior route in the extraction of many intraocular foreign bodies. Although I was originally trained to remove most intraocular foreign bodies by the anterior route after first drawing them into the anterior chamber with the magnet, I have recently removed more such foreign bodies posteriorly.

I like to ring the incision with electrolytic punctures. Because some foreign bodies which were originally considered nonmagnetic proved to be magnetic after enucleation, and because my associates and I have apparently had success in similar cases with use of the Berman localizer, I am convinced that in all cases of doubt this added means of accurate localization of foreign bodies should be employed. We have so far used this instrument in 10 cases at the New York Eye and Ear Infirmary, and in 4 cases we believe the localizer has been of material assistance in the operation.

Even though the roentgenologic localizing method and the Comberg technic with the contact glass are excellent, more exact localization is sometimes desirable when a foreign body is enmeshed in the tissue.

**Paralysis of the Superior Rectus Muscle, Exophthalmos, Pseudoptosis and Fibrosis of Inferior Rectus Muscle Following General Anesthesia.** DR. CONRAD BERENS and CAPTAIN GERALD FONDA, Medical Corps, Army of the United States.

This article will be published in full, with discussion, in a future issue of the ARCHIVES.

**Evaluation of Results in a Series of Corneal Transplants.** DR. R. TOWNLEY PATON.

The operation for the removal of corneal scars has now well stood the test of time. No longer may one doubt the permanence of improvement in sight obtainable by corneal transplantation in carefully selected cases. Corneal surgery has met all the vicissitudes and platitudes to which in the past cataract surgery was subjected. Let the young ophthalmic surgeon be taught that this operation is simple, easy to perform and often successful in restoring sight.

The various technics are easily acquired. Although every surgeon is likely to modify the operation in one way or another, certain principles must be strictly adhered to.

1. The donor's graft must be traced and carefully dissected. Whether a square or round graft or one of some other shape is used makes little difference except from the cosmetic point of view, so long as the edges are even and smooth.

2. An exact tracing (never smaller than the donor's graft) on the recipient's cornea and an equally careful dissection are essential, special care being given of course to the internal structures of the eye, the iris, lens, etc.

3. Beveling should be avoided as much as possible, in either the donor's or the recipient's eye, as it only leads to an imperfect fit.

4. Sutures should be inserted before the anterior chamber is penetrated. The sutures should be placed as close to the traced edges as possible.

5. Two sutures are preferable to one because they are easier to tighten, more even distribution of pressure is obtainable, especially when there is a tendency to overriding of one edge of the graft, and there is less danger of complication if one suture is accidentally cut.

6. Use of conjunctival flaps invariably leads to complications and should be discouraged.

7. The donor's eye should be carefully selected, and young eyes are probably better than old eyes. Until corneas are obtainable in large quantities, it has been the tendency to use only healthy-appearing corneas, regardless of race, blood group or age.

8. As yet little is known about the problem of corneal vascularization and its prevention. Roentgen ray therapy, given a day or two after

operation, has been tried, but my experience is limited to only a few cases.

9. Postoperative care of the graft offers one of the greatest avenues for research in the future.

In a limited experience of 50 cases carefully studied at the Manhattan Eye and Ear Hospital, and another 50 cases studied in Baltimore and at the Flower–Fifth Avenue Hospital several years ago, my results are encouraging. In nearly all cases sight was improved. In 3 cases the eyes were lost. In 4 cases serious postoperative conjunctivitis developed, which spoiled what might have been an excellent result. In only 2 cases was vision of 20/30 obtainable—improvement in 1 case being from 10/200 and in the other from 20/200. The average improvement was from ability to count fingers at 2 feet (60 cm.) to visual acuity of 20/200.

One patient had a particularly successful graft done on one eye, vision improving from perception of hand movements to 20/50. At the end of three years the graft is beginning to cloud over. The other eye has had four grafting operations, a cataract extraction and a trephination; this eye is now ready for a fifth operation, as the tension is down and vision as good as when treatment was started, several years ago.

DISCUSSION

DR. RAMÓN CASTROVIEJO: As Dr. Paton said, keratoplasty is an operation with which all ophthalmologists should become acquainted because, although it requires a high degree of accuracy, it can be performed by any one who has been well trained in ophthalmology. At the Institute of Ophthalmology of the Columbia Presbyterian Medical Center, the residents perform keratoplasties, with results comparable to those obtained by men who have had more experience in this type of surgery.

In properly selected cases excellent visual improvement may be expected. In favorable cases the average vision obtained is generally better than 20/50. It is not infrequent to obtain vision of 20/20. In some of the cases in which operation has been performed at this institute vision of 20/15 has been obtained. Some of the patients operated on for corneal transplantation have been able to engage in occupations requiring a great deal of use of the eyes, such as bookkeeping; other men with corneal transplantations have been inducted into the armed forces, with normal vision.

Dr. Paton mentioned keratoplasty for cosmetic purposes. It has been the experience of my associates and myself that in a small percentage of cases, perhaps in no more than 1 per cent, is corneal transplantation needed for cosmetic purposes. For such purposes Dr. Paton prefers the round transplant. I prefer the square one for I feel that it is easier to graft. If the transplant remains clear, the shape of the graft can be seen with difficulty because the scars are almost invisible a few months after the operation. On the other hand, if the transplant becomes opaque, the shape of the graft does not matter because it looks bad anyway.

I agree with Dr. Paton in regard to beveling. In my opinion beveling of the donor's graft is not necessary, but I believe it is desirable to have a slight beveling of the endothelium of the host's cornea in order to counteract the tendency of the endothelium to roll inward and thus leave a gap in the posterior surface which will become filled with fibrin. The conditions for adhesion of the iris to this gap are favorable if the pupil is not fully dilated. The slight beveling of the endothelium brings about a better approximation of the posterior layers of the graft and the cornea of the host, so that early restoration of the anterior chamber is facilitated and formation of anterior synechias and subsequent nebulosity of the graft, and in some cases secondary glaucoma, prevented.

Contrary to what Dr. Paton has stated, namely, that two sutures are better than one to hold the graft in position because they make a more uniform pressure, it has been my experience when I used two sutures that one of them might press on the transplant more than the other and thus interfere with the even cicatrization of the graft. This unevenness of pressure is prevented by use of a continuous suture.

At the Institute of Ophthalmology corneas taken from Negroes have been used in keratoplasties on white patients, and vice versa. The results have been similar to the results in cases in which white patients and Negroes had transplants of donor material obtained from persons of their own race. The work of Elschnig, Filatov, Thomas and myself has shown that the blood group has no bearing on the success or the failure of keratoplasty.

Dr. Paton mentioned the use of roentgen radiation two or three days after the operation to prevent vascularization of the graft. In my experience I have not noticed vascularization of the graft until the third or fourth week after corneal transplantation. If roentgen radiation is to be employed to prevent vascularization of the graft, it should be begun no sooner than two weeks after the operation. To use roentgen radiation only two or three days after operation encourages the formation of anterior synechias with subsequent opacity of the graft and possibly secondary glaucoma.

In the case Dr. Paton reported in which a corneal transplantation had been performed on a cornea with calcareous degeneration, probably more benefit would have been derived from a superficial keratectomy than from a corneal transplantation. Similar cases in our hands resulted in failure when a corneal transplantation was performed, and in a high percentage of cases successful results were obtained after superficial keratectomy.

The problem of corneal transplantation cannot be discussed in a few minutes. There are many points that would require extensive discussion, such as the indications for keratoplasty. The indications for this type of operation are definite; at the Institute of Ophthalmology my associates and I have been able to tell with an accuracy of almost 99 per cent which cases are favorable for corneal transplantation and which are not. It has also been possible to foretell the cases in which a high percentage of transparent grafts were likely to result and those in which the transplant would become nebulous or opaque. Once the indications for keratoplasty have been well established, it would be as useless to operate in a case in which no hope of improvement of vision was offered as it would to operate in a case for cataract when the perception and projection of light are defective.

It is regrettable that the lay publications have dramatized this subject so extensively, stimulating false hopes among the public, who expect this operation to be effective with all kinds of conditions and who, the more it is publicized, will hope for miracles, no matter how accurately the indications for this type of treatment are explained to them.

By now the possibility of dramatization of this problem has almost exhausted itself, and in the future it is to be hoped that members of the medical profession will be left alone to work without interference for the benefit of all.

DR. CONRAD BERENS: I am deeply interested in this splendid presentation, as I am sure all have been, but I am disturbed by the number of patients who come with false hopes of obtaining cure for blindness. How many patients considered sufficiently blind to be institutionalized, or needing guidance by a Seeing Eye dog, have been benefited by corneal transplantation to a point at which they were able to engage in occupations for which good vision is usually needed? Might not these same patients have been equally benefited by optical iridectomy or superficial keratectomy?

My experience with the New York Association for the Blind and a home for blind babies, as well as my long association with the work of the American Foundation for the Blind and the National Society for the Prevention of Blindness, makes me believe that the answer to this question is important. I have yet to see a single patient in the category of the blind who was benefited by a corneal transplant and could not have been helped almost as much by optical iridectomy or keratectomy. Certainly, the statement that 100,000 patients in the United States could be made to see through this operation is a bit fantastic, and I am glad that Dr. Paton stressed that too much had been made of this problem in the newspapers and in other publications.

This leads to the case of calcareous deposits which Dr. Castroviejo mentioned. I asked Dr. Paton whether he had here a section of the cornea, for it is my impression that most of these calcareous deposits are superficial, and I have had good results with superficial keratectomy in cases of this condition.

I agree with Dr. Paton on the question of sutures, for I have been interested in the use of two sutures instead of one, one white and the other black, the two being locked in the episcleral tissue with a small strip of plastic material. With this technic I believe I can equalize the tension more satisfactorily, and the manipulation of the sutures is much simpler.

I should like to know Dr. Casteroviejo's technic for making a square incision, that is, how he obtains an approximately straight upper edge where the keratome is introduced.

DR. R. TOWNLEY PATON: I agree with Dr. Berens about the number of people who are actually blind and can be helped by this operation.

With regard to Dr. Castroviejo's point I feel that a round window more closely resembles the pupil and that as the opacity of the cornea extends well beyond the central area in a majority of cases, trephination should be used wherever possible. This holds true particularly for women.

With regard to cutting the edges, I cannot state definitely that some beveling is not obtained, but I certainly do not try to bevel after I have once punctured the anterior chamber. It might be well always to use a cataract knife to puncture the anterior chamber, because the ordinary keratome and the Agnew knife are angled in such a way that it is almost impossible to make a right-angled puncture into the anterior chamber. I have used a modified keratome with satisfactory results.

DR. RAMÓN CASTROVIEJO: In answer to Dr. Berens, the keratome should be used only to make an opening into the anterior chamber, through which one of the blades of the scissors is introduced in order to complete the corneal incision. No attempt should be made to cut down with the keratome perpendicular to the cornea because in this position the keratome may injure the lens. Of course, this does not apply to the case of the donor, as it does not matter whether his lens is injured.

**Traumatic Subconjunctival Dislocation of the Lens: Report of a Case.** DR. DONALD WEEKS BOGART.

The patient was seen five days after an automobile accident in which the pelvis and the occipital bone were fractured. Vision in the right eye was reduced to perception of light. There was a cystic mass the size of a pea under the unlacerated portion of the conjunctiva just anterior to the insertion of the superior rectus

muscle. The iris was drawn up, the appearance suggesting an operative wound. With ultraviolet light the mass was fluorescent, proving that it was the lens.

The lens was easily removed through the conjunctival incision; the iris was excised where it was prolapsed, and the sclera was closed. The postoperative course was uneventful, and on the patient's discharge, a month later vision had improved to perception of hand movements, although the vitreous had not yet cleared of hemorrhage resulting from the accident.

The causes of lenticular dislocation of this type are discussed. The reasons for presentation of this case are as follows: (1) the interesting nature of the diagnostic problem and the arrival at the diagnosis on the basis of examination with ultraviolet light; (2) the speedy recovery following removal of the lens, absorption of which would have taken considerable time and (3) the necessity for closure of the sclera and of inspection of the ciliary body.

**Binocular Papilledema in a Case of Torulosis (Pathogenic Yeast Infection) Associated with Hodgkin's Disease.** DR. MARTIN COHEN.

This paper was published in full in the December issue of the ARCHIVES, page 477.

**Meningioma of the Sphenoidal Ridge: Report of a Case.** DR. RUDOLF AEBLI.

A 7 year old boy had a history of gradual protrusion of the left eye, of one year's duration. The eye was pushed down and in, and abduction and elevation were limited. Vision was 20/20 in each eye, and examination of the fundus revealed nothing significant. Roentgenograms taken at various intervals ultimately showed bony changes in the left sphenoid ridge and around the left superior sphenoid fissure. The diagnosis was neoplasm of the middle fossa with extension into the orbit. A left frontoparietal craniotomy, performed by Dr. Joseph King in July 1939, revealed a firm mass, the size of a silver dollar, adherent to the dura over the area of the left sphenoid ridge. In November 1939 a left temporal transconjunctival approach to the retroorbital area was made, and two globular masses, one measuring 2 cm. and the other 3 cm. in diameter, were removed. Adhesions to the lids were produced. Examination of tissue showed that both the orbital masses and the intracranial mass had the characteristic structure of a meningioma.

In November 1940 the boy was readmitted to the hospital with an increase in the exophthalmos, papillitis and progressive loss of vision. Roentgenograms showed dense bony shadows in the sphenoid ridge, the roof of the orbit and the lateral walls and floor of the orbit. A second frontoparietal craniotomy was performed by Dr. Joseph King, and the sphenoid ridge and the roof and lateral wall of the orbit were removed. In January 1942 the left orbit was exenterated. The latest roentgenograms showed dense bony shadows in the maxillary area and in the malar bone on the left side. The patient has now been followed for six years, and, except for the local symptoms and signs about the left orbit, the boy is well.

In cases of slowly progressive unilateral exophthalmos with limitation of abduction and elevation, frequent stereoscopic roentgenograms of the orbit should be taken. An early intracranial approach is essential, for once the tumor has invaded the bone and extensive bony infiltration is present, it is impossible to remove the osteoma completely.

DISCUSSION

DR. JOSEPH E. J. KING: This is the youngest person on whom I have ever operated for the meningioma of the sphenoid ridge. The tumor usually occurs in older people. This tumor invaded the bone and thickened it greatly. At the time Dr. Aebli and I first saw the boy we did not know the details in the case and removed the roof of the orbit and the frontal ridge, as advised by Dr. Gilbert Horrax. If I am not mistaken, this tumor also invaded the orbit, forming a dumbbell-shaped mass. The tumor involving the bone extended slowly, as Dr. Aebli described, entered the base of the wing of the sphenoid bone and extended into the left malar bone, and possibly backward into the bones forming the base of the skull. After exenteration of all the contents of the orbit, we later removed the left malar bone and completely uncovered the antrum, covered it with cutaneous flaps and inserted a drain in the antrum. Shortly after this procedure an opening was made into the inner wall of the antrum through the nose to provide drainage. When the contents of the orbit were completely removed and the optic nerve was divided near its entrance to the orbit, there followed a considerable flow of cerebrospinal fluid, and we feared infection of the meninges might occur. The amount of fluid which escaped in a day was enormous, the fluid wetting the dressing thoroughly and running down the patient's cheek. We filled the orbit partly with a sulfonamide powder and packed it with gauze, and slowly and gradually the leakage ceased, without development of meningitis. One of our colleagues remarked that we were wasting time on this boy; but the child has lived for several years, and he is still getting along well. I think that after all the expenditure of time was worth while.

DR. JAMES W. SMITH: The report of Dr. Aebli is a reminder that meningioma must be fairly common. Ten years ago Dr. Cohen reported a case before this section; Dr. Knapp reported 2 cases before the American Ophthalmological Society in 1938, and Dr. Kirby pre-

sented 1 case in discussion; I presented a case before this society in 1939, and Dr. Givner has 2 cases under observation in which the diagnosis has been verified roentgenographically. Roentgenography is invaluable, and yet a flat roentgenogram made in my case and in Dr. Knapp's first case failed to establish the diagnosis. A clinical fact worth mentioning is that stereoscopic roentgenograms are essential for accurate localization.

Dr. Aebli did not mention the diagnostic point with regard to suprazygomatic swelling which I emphasized in my paper (Meningioma Producing Unilateral Exophthalmos, ARCH. OPHTH. 22:540 [Oct.] 1939). The swelling was evident in the photograph of his patient; it is a valuable clinical sign of earlier appearance than the exophthalmos, which, as Dr. Aebli stressed, was slowly progressive, painless, nonpulsating and unilateral.

As Dr. King stated, most meningiomas of the sphenoid ridge occur in middle-aged patients, and the extensive involvement observed in this child was unusual. I had the good fortune to communicate with the late Dr. Harvey Cushing, who was the pioneer in meningioma research. He stressed that in most of his cases the tumor occurred in females and on the left side. He also observed in his series of cases of meningioma that most of the women had the suprazygomatic fulness but dressed their hair over the swelling in such a manner that the clinician missed an important diagnostic sign. I profited by Dr. Cushing's comment and had the photograph of my patient taken with her hair combed up and tied with a ribbon.

It is almost impossible for a neurosurgeon to remove all the area of hyperostosis. In my case about seven eighths of the tumor was removed, and the exophthalmos receded 2 mm. During the past year the exophthalmos has slowly recurred, but vision is normal. I plan to do a tarsorrhaphy to narrow the width of the palpebral fissure as the advanced age of my patient would preclude another major neurosurgical operation.

DR. ALFRED KESTENBAUM: All should be grateful to Dr. Aebli for his drawing attention to this important condition. Sometimes the ophthalmologist is able to arrive at the diagnosis early. In May 1942 I saw a woman approximately 56 years of age with slight exophthalmos of the left eye, of only 1 mm. There was slight paresis of the left superior rectus muscle; motility in upward gaze was only 1 mm. less than that of the other eye, but the diplopia was significant. For a white object there was a relative central scotoma, which extended downward. For a red object the entire lower half of the field, including the center, was defective. Vision was reduced to 20/100. The temporal part of the disk was slightly pale. All these signs pointed to the diagnosis of a retrobulbar space-taking process, apparently in the posterior upper part of the orbit. I made a tentative diagnosis of meningioma of the left sphenoid ridge. One month later exact measurement revealed slight but definite deterioration in every aspect. The exophthalmos was 2.5 mm.; the elevation of the left eye was a little more restricted (defect about 2 mm.); in addition, there was slight ptosis; vision was slightly less than before, and the scotoma was increased. I made a diagnosis of progression of the meningioma and advised operation. Permission, however, was refused, and I saw the patient three months later, in September. Visual acuity was now reduced to ability to count fingers at 1.5 meters. The scotoma for white objects was absolute. The elevation of the eye was still more restricted and the degree of exophthalmos a little increased. An exploratory operation, by Dr. Leo Davidoff, revealed a meningioma of the left sphenoid ridge, and this was removed. After operation the exophthalmos was less pronounced, but vision remained unchanged. It is not yet two years since the operation, so that a definite prognosis cannot be given; but up to the present, aside from the decreased vision, the patient is well.

DR. RUDOLF AEBLI: Dr. Smith, the roentgenograms were stereoscopic, and taken by Dr. F. M. Law.

With regard to the question whether the fulness over the left zygoma is an early sign, I suspect that by the time fulness appears the meningioma will already have invaded the retrobulbar area or the temporal fossa. I do not see how fulness here could be an early sign, for it must be due to edema or swelling, but it is a definite sign.

**Metastatic Orbital Tumor with Exophthalmos: Report of a Case.** DR. DONALD BALL.

A white man aged 70 complained of protrusion of the left eye with diminution of vision, of only one week's duration. His health had been good until two months prior to admission to the hospital, when he noted occasional expectoration of blood-stained sputum; there was loss of weight of 20 pounds (9.1 Kg.) in the month before admission, and for three weeks prior to entrance to the hospital there had been slight swelling of and pain in the left cheek.

Visual acuity was 20/40 in the right eye and 3/200 in the left eye. There was pronounced proptosis of the left eye, with limitation of motion in all directions. The corneal apex pointed downward. A fulness was felt below the globe and inside the orbital rim. The globe was tender, and the tension was high. The pupil was dilated, and its reactions were sluggish. The fundus showed dilated and tortuous veins and early papilledema. There was notable constriction of the visual field. The right eye was normal.

The patient was extremely emaciated. The final clinical diagnosis was bronchogenic carcinoma with metastases to the left orbital area and to the brain.

Twelve days after admission removal by aspiration of a specimen for biopsy from the inferior temporal region of the left orbit revealed a firm mass, about 10 mm. in depth, against the posterior wall. A week later, because of the rapid deterioration of the left eye, the contents of the orbit were exenterated. A dense tumor mass was encountered just inside the rim of the orbit. The posterior, inferior and superior walls of the orbit were eroded, and a large amount of tumor tissue remained in the posterior portion of the orbit.

The postoperative course was downhill, and the patient died three weeks later. Autopsy revealed a primary squamous cell carcinoma of the left maxillary sinus, which had invaded, through direct extension, the left orbital fossa and, subsequently, the anterior cranial fossa. Metastases were present in the lungs.

This case was thought of sufficient interest for a report because the exophthalmos was unilateral, the cause presented a diagnostic problem, the operation was difficult and the condition was rare.

DISCUSSION

DR. DONALD WEEKS BOGART: The primary fact which misled Dr. Ball and me was the medical report of a lesion in the lung; we concluded that the patient had a primary bronchogenic carcinoma. The specialists in nose and throat disease did not have a chance to look at the antrum. If they had, I am certain that we should have been put on the right track.

During the operation, the bone in the roof of the antrum and the roof of the orbit were observed to be very soft; it is surprising that this condition did not show in the roentgenogram. On careful probing backward we believed that we encountered brain tissue, and autopsy verified this. The tumor had extensively invaded the cerebral cavity and the antrum. I feel that the final diagnosis should not be made without consultation.

# News and Notes

EDITED BY DR. W. L. BENEDICT

## GENERAL NEWS

**The National Society for the Prevention of Blindness, Inc.**—A prize of $500 is offered by the National Society for the Prevention of Blindness, Inc., 1790 Broadway, New York 19, for the most valuable original paper adding to existing knowledge about the diagnosis of early glaucoma or the medical treatment of noncongestive glaucoma. This award will take the place of two separate prizes of $250 each which were announced some time ago.

Papers may be presented by any practicing ophthalmologist in the Western Hemisphere and may be written in English, French, German, Italian, Spanish or Portuguese. Papers written in the last four languages should be accompanied with a summary in English.

**Ophthalmologic Seminar, Emory University School of Medicine.**—An ophthalmologic seminar, sponsored by Emory University School of Medicine, honoring the memory of Dr. Abner Wellborn Calhoun, M.D., LL.D., who was born April 16, 1845, will be held in Atlanta, Ga., April 19 to 21, 1945. Dr. Calhoun was the first professor of ophthalmology of Emory University and a pioneer in southern ophthalmology. All who are interested in ophthalmology are invited to attend as guests of Emory University.

The guest speakers will be Dr. W. L. Benedict, Dr. John Dunnington, Dr. Harry Gradle, Dr. Parker Heath, Dr. Walter I. Lillie, Colonel Derrick Vail and Dr. Frank Walsh.

# Directory of Ophthalmologic Societies *

## INTERNATIONAL

### International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

### International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

### International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

### Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

## FOREIGN

### All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

### British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

### Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

### Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

### Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

### German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

### Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

### Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

### North of England Ophthalmological Society

President: Mr. John Foster, 45 Park Sq., Leeds.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

### Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

### Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

### Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.

### Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

### Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

### Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Prof. Moacyr E. Alvaro, Consolação 1151, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

SCOTTISH OPHTHALMOLOGICAL CLUB

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

SOCIEDADE DE OFTALMOLOGIA E OTORRINOLARINGOLOGIA DE RIO GRANDE DO SUL

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

## NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: Philadelphia. Time: June 18-22, 1945.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

## SECTIONAL

### Academy of Medicine of Northern New Jersey, Section on Eye, Ear, Nose and Throat

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

### Central Wisconsin Society of Ophthalmology and Otolaryngology

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

### New England Ophthalmological Society

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

### Pacific Coast Oto-Ophthalmological Society

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

### Pudget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. L. Bull, 1215–14th Ave., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

### Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

### Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. L. D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

### Sioux Valley Eye and Ear Academy

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

### Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

### Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

### Southwestern Michigan Triological Society

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

### Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

## STATE

### Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

### Colorado Ophthalmological Society

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

### Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

### Eye, Ear, Nose and Throat Club of Georgia

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

### Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

### Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

### Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

### Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val. H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

### Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

### Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

### Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

### Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N. St., Lincoln.

### New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. B. E. Failing, 31 Lincoln Park, Newark.
Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

### New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

### North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

### North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

### Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

### Pennsylvania Academy of Ophthalmology and Otolaryngology

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

### Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

### South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

### Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

### Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

### Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

### Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.

Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

## LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.

Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.

Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.

Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.

Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.

Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.

Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.

Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.

Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn 16.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.

Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.

Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.

Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.

Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.

Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.

Time: 6:30 p. m., third Tuesday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.

Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

### Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

### Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Cecil W. Lepard, 1025 David Whitney Bldg., Detroit 26.
Place: Club rooms of Wayne County Medical Society.
Time: First Wednesday of each month, November to April, inclusive.

### Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.
Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

### Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

### Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

### Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

### Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

### Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

### Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

### Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.
Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

### Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

### Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

### Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

### Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

### Milwaukee Oto-Ophthalmic Society

President: Dr. Leon H. Guerin, 324 E. Wisconsin Ave., Milwaukee 2.
Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.
Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

### Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

### Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

### Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

### New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

### New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

### New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Thomas H. Johnson, 30 W. 59th St., New York.
Secretary: Dr. Wendell L. Hughes, 131 Fulton Ave., Hempstead, N. Y.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

### New York Society for Clinical Ophthalmology

President: Dr. Milton Berliner, 57 W. 57th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

### Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

### Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

### Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

### Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

### Pittsburgh Ophthalmological Society

President: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Secretary: Dr. Robert J. Billings, 509 Liberty Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

### Reading Eye, Ear, Nose and Throat Society

President: Dr. Michael J. Penta, 312 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

### Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

### Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

### St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.
Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

### San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

### San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

### Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

### Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

### Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

### Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

### Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

### Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.
Secretary-Treasurer: Dr. John Lloyd, 1218–16th St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

### Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.